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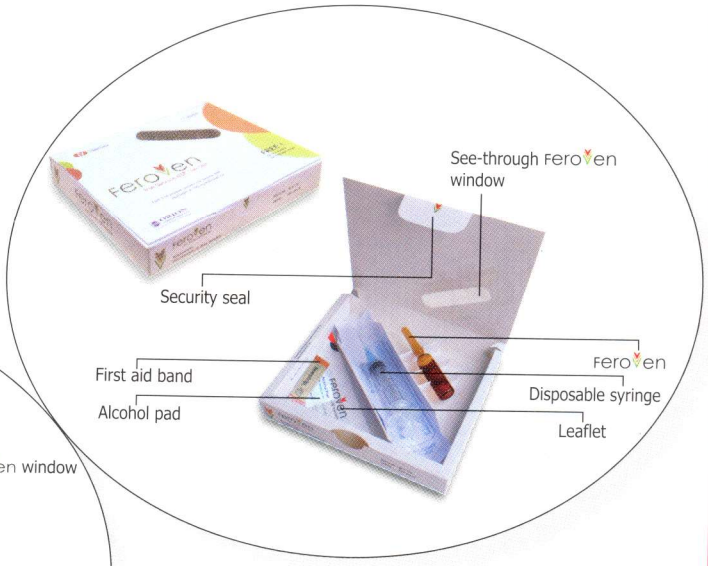

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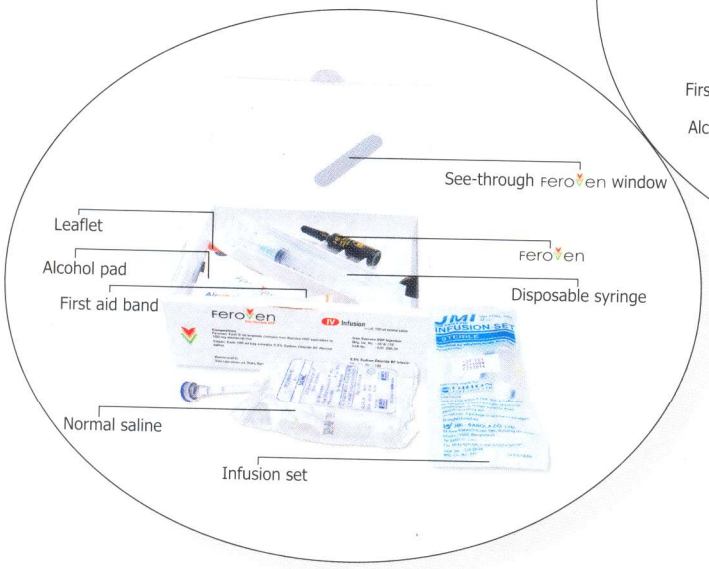

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"The ORION", is one of the leading Medical Journals of the country which has been published successfully for the last 11 years. "The ORION", not only meets the quantity but also satisfies the quality of the publication by peer review, reference input, text index, latest medical and scientific news and information which is more user friendly to the authors, readers, members and subscribers.

"The ORION" today is one of the mostly accepted journals in Bangladesh with highest number of publication. A new website (www.orion-group.net/medicaljournal) is continuing with complete indexing of "The ORION" Medical Journal from 2010. This issue (Volume 33, Issue 2) comprises of 02 original articles, 05 review articles and 01 case report.

Editorial (P-738) of this issue "The development of neurosurgery in Bangladesh" states the history and prospects of neurosurgery in perspective of Bangladesh.

The first original article (P-739) "Cardiovascular risk factors & complications in patients with ESRD on maintenance haemodialysis" reveals BP, Hb level & glycaemia are the three main factors to develop cardiovascular complications of patients with ESRD on maintenance haemodialysis.

Second original article (P-742) "Prevention and control of rheumatic heart disease among school aged children (5-15 years) in a rural area of Bangladesh" analyzes the prevalence & prevention of RHD, and concludes in the importance of proper diagnosis of RHD.

First review article (P-745) "An overview and update management of myelodysplastic syndrome" introduces a novel therapy option for better prognosis of myelodysplastic syndrome.

Second review article (P-748) "Multiple myeloma: A review" briefs about multiple myeloma and states about the great research scope to discover newer drugs to improve survival or cure of myeloma patients.

Third review article (P-752) "Cough variant asthma" highlights chronic non-productive cough as the precursor of asthma, but remains as diagnostic challenge to treat.

Next review article (P-758) "Dementia: Management update" denotes the type & stage of dementia, & evaluates multidirectional treatment modalities in different stages.

Last review article (P-764) "Resistant hypertension: An approach to its management" states about the careful evaluation of the patient with resistant hypertension to confirm the diagnosis and to exclude factors associated with pseudo-resistance hypertension.

Case report (P-768) of this issue "A case report: Healthy pregnancy following removal of dermoid cyst" shares the experience of successful removal of dermoid cyst following healthy pregnancy of the patient. Author also advises early diagnosis, early laparotomy & histopathology of dermoid cyst can make a patient almost cure.

Further opinion and suggestions are highly encouraged for development of "The ORION". The journal is freely available at www.orion-group.net/medicaljournal or www.orion-group.net/journals for contributing towards the advancement of public health and medical research. For reproducing multiple copies of any of articles published in "The ORION", please e-mail:orionjournal@yahoo.com/ msdorion@yahoo.com/ journal@orion-group.net & mention the article title, author's name, volume, page number, year of publication and most important the purpose for reproducing.

May the Almighty bless all in the spirit of good health.

DR. MOHAMMAD FERDOUS RAHMAN SARKER
Chief Editor
The ORION Medical Journal

The Editorial Board

The development of neurosurgery in Bangladesh

Alam S[1], Khair A[2]

The ORION Medical Journal 2010 May;33(2):738

Bangladesh has an average life expectancy of approximately 60 years. The chances of dying between the ages of 15 and 60 years are more than 1 in 4. Health remains an important goal and instrument of development in this ever-growing nation.The beginning of neurosurgery is not very new in Bangladesh. It started its expedition following the liberation war in 1971 in IPGMR, under the guidance and concentration of Ex. Professor Rashid Uddin Ahmed. Inspired by him, others like Professor Ata Elahi Khan and Professor L. A. Quadery had established neurosurgery ward respectively in DMCH and CMCH. Since then they had been working hard togethetr to establish to increase the number of beds in ward, and motivated, inspired and trained new doctors to consider neurosurgery as career path. In the mean time they also established neurosurgery teaching in under-graduate level.

At that time private neurological practice was rare and undeveloped. But after a long dormant period of time, in the year 1998 neurosurgery post graduate courses started both in IPGMR and DMCH simultaneously, which has then gradually expanded to CMCH and MMCH too. Following the upgradation of post graduate courses and rapid development of skilled Neurosurgeons; neurosurgery diagnostic facilities like CT Scan, MRI, Myelography were also becoming available gradually. At that time Neurosurgeons most commonly deals with head Injuries, spinal injuries, brain tumor, spinal tumor, PLID etc.

Following year 2000, there was a rapid progression of neurosurgery further both in private and in government level. At the same time post graduation courses also expanded much more ever than the past. Hence the neurological facilities has been becoming more available for all income level persons like the richer and poorer. Now we have CT-Angio, DSA, Transcranial doppler, good quality Microscope facilities in Bangladesh. With the available investigations, diagnostic facilities, operative facilities and good neuroanesthesia; Neurosurgeons are now also developed their skillness in vascular neurosurgery, pediatric neurosurgery, endoscopic neurosurgery and steriotactic neurosurgery.

Now all types of neurosurgical cases can be dealt in BSMMU, DMCH, and other equiped clinics and hospitals. We are still in lacking of Gamma knife radiosurgery, Neuro-navigation, Image guided surgery for super management of patient. We are no more lagging behind our relative countries. By continuous suitable training from home and abroad, we are taking hard step to decrease mortality and morbidity of neurological patient, which is a common issue for our society. Now promising new doctors are continuing to learn and devote in taking neurosurgery following residency postgraduation in BSMMU, MS courses and more other postgraduation courses in respective Hospitals. Neurologic trainees and the Neurologists are now also much more enthusiast to do clinical research.

Neurosurgeons now-a-days are dealing with critical cases like head injuries, brain disorders, spinal pathologies and peripheral nerve problems. We are also hopeful that, very soon we would be able to achieve and develop our standard of neurosurgery to an International level by our determination and continuous effort, and by suitable and update learning, teaching and training. Though, Government and private sectors are now more attentive regarding to the development of neurosurgery as an emergency and critical care. But it is still need more neurologic specialized hospital in Bangladesh. Anyhow, throughout our country hospitals for cancer and heart disease have sprung up. Then, why not one for neurologic diseases too?

All the tributes and respects to our first generation neurosurgeons, who have blessed us by their spirit to develop neurosurgery in Bangladesh.

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Cardiovascular risk factors & complications in patient with ESRD on maintenance haemodialysis

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The ORION Medical Journal 2010 May;33(2):739-741

Abstract

The present cross-sectional study was carried out at BSMMU, Dhaka Medical College Hospital (DMCH), National Institute of Kidney Diseases & Urology (NIKDU) and Kidney Foundation between July 2005 to June 2007 to find out the risk factors of Cardiovascular Complications in End Stage Renal Disease (ESRD) patients on Maintenance Haemodialysis. Patients of both sexes with age ranging from 18-59 years and getting at least 8 hours of Haemodialysis per week for the last 3 months were the enrollment criteria. A total of 126 such patients were included in the study. The test statistics used to analysis the data were Chi-square test or Fisher's Exact Probability Test and Student's t-test. Of the 126 patients 61.1% developed some types of cardiovascular complications. In terms of type of complications 63.6% of the patients had LVH, 23.4% had ischemic heart disease (IHD), and 10.4% had congestive cardiac failure (CCF) and 2.6% Cardiomyopathy. Over 96% patients were hypertensive, followed by 46.8% diabetics and 42.1% smokers. Presence of hypertension, diabetes, family history of diabetes and hypertension were observed to be significantly higher in patients, who develop cardiovascular complications ($p < 0.05$). It is concluded that Cardiovascular Complications (CVC) are very common in ESRD patients on Maintenance Haemodialysis (MHD). Further well designed studies needed to find out the risk factors for development of CVC in ESRD.

Key words

Chronic kidney diseases, Cardiovascular complication.

Introduction

Cardiovascular disease is the principal cause of mortality in patients with chronic renal disease undergoing haemodialysis.[1] Patients with End Stage Renal Disease (ESRD) are at high risk of developing cardiovascular complications, which is considered the leading cause of mortality & morbidity in dialysis patients accounting for 40 to 50% of deaths.[2] Despite many technical advances in the field of dialysis, patients undergoing Renal Replacement Treatment (RRT) display a significantly lower life expectancy compared with their counterparts in the general population.[3] According to the records of last 15 years, 50% of these patients died from cardiovascular complications every year.[4] Aortic stiffness & Left Ventricular Hypertrophy (LVH) are predictors of mortality in Haemodialysis (HD) patients.[5] Coronary artery calcification is common, severe and significantly associated with Ischemic Cardiovascular Disease in adult ESRD patients.[6] Other study identified clinical predictors of survival of diabetic End Stage Renal Disease (ESRD) patients on haemodialysis, including age at haemodialysis initiation, nutritional status, dyslipidaemia and existence of cardiovascular complications.[7] Cardiovascular diseases are the leading cause of death; Volume overload, Anaemia, Hypertension, Arteriovenous fistula, Uraemia related myocardial cell injury all contribute to the development of Ischemic Heart Disease & Congestive Heart Failure.[3] Although Hypertension has been considered as a major risk factor in End Stage Renal Disease (ESRD) patients, its influence on CV prognosis remains controversial.[8] Haemodialysis patients with cardiovascular disease exhibited higher levels of Triglyceride, VLDL-cholesterol, total Cholesterol, LDL-cholesterol and lower levels of HDL-cholesterol than those without cardiovascular disorders.[9] Patients who die from cardiovascular complications have higher levels of Triglycerides.[10] In Diabetic Haemodialysis patients, cardiovascular complications & cardiac death are associated with low HDL-cholesterol values.[9] The percentage of haemodialysis patients with Coronary calcifications has also been found to be 10 fold higher compared to age matched healthy controls, using Computed Tomography.[11] In the general population high Blood Pressure (BP) is related with an increased risk of cardiovascular disease & high total mortality, while its regulation has been associated with decreased cardiovascular risk.[12] From the background informations it appears that with the increase of Diabetes, Hypertension the prevalence of Chronic Kidney Disease (CKD) is also alarmingly going up with consequent increase in End Stage Renal Disease (ESRD). ESRD poses patients at high risk of developing cardiovascular complications, which is considered as the leading cause of mortality & morbidity in dialysis patients accounting for 40 to 50% of deaths. Despite many technical advances in the field of dialysis, patients undergoing chronic Renal Replacement Treatment (RRT) display a significantly lower life expectancy compared with their counterparts in the general population. The purpose of the present study is designed to observe the Cardiovascular Complications (CVC) of End Stage Renal Diseases (ESRD) patients on Maintenance Haemodialysis (MHD).

Material & method

126 ESRD patients on MHD who were on MHD for $\geq$ 3 months in the Department of Nephrology of DMCH, BSMMU, NIKDU, and KF during the period of July 2005 to June 2007 were included in this study. All the patients were dialysed by A-V fistula with 2 to 3 times per week for 4 hours per session of HD. The patients were evaluated by taking clinical history, physical and clinical examination, biochemical investigation like Hb, Blood Urea, Serum creatinine, S. electrolyte, S. calcium were estimated by standard method. X-ray Chest P-A view, ECG, Echo was also done. All patients were followed up for two years.

Statistical method: Data were processed & analyzed using computer software SPSS (statistical package for social science).

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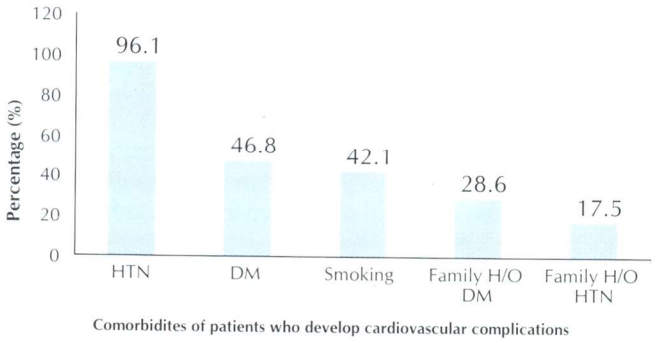
The test statistics used to analyse the data were student's t test (for comparing of data presented in quantitive scale), Chi-square test or Fisher's exact probability test. For any analytical test, the level of significance was 0.05 & P-value < 0.05 was considered significant.

Result

Out of 126 patients on Maintenance Haemodialysis (MHD), the mean age was 48.44 ±12.62 years & the lowest & highest ages were 18 & 59 years respectively. Patient age 50 yrs or higher was found to develop more cardiovascular complications compared to those below 50 yrs of age (80.5% Vs 19.5%) (P<0.001) & male (54%) sex was found to be associated with the development of cardiovascular complication more frequently than female (46%). 126 patients 38.1% was service holder, 33.1% were house wife, 20.6% small businessmen, 4.8% student & 3.2% was unemployed. Distribution of patients by their causes of ESRD shows that GN (42.9%), was the leading cause of ESRD followed by diabetes (31.7%), HTN (24.6%) & other (0.8%). Among 126 pts only 77 (61.1%) developed one or more Cardiovascular complications & the remaining 49 (38.9%) didn't develop any Cardiovascular complications. Over 63% of pts had LVH, 23.4% IHD, 10.4% CCF & 2.6% Cardiomyopathy (Table 1).

Table 1: Distribution of patients by cardiovascular complications (n = 126)

Cardiovascular complications	Frequency	Percentage (%)
LVH	80	63.3
IHD	30	24.0
CCF	14	11.1
Cardiomyopathy	02	1.6



Graph 1: Distribution of patients by risk factors of CV complications

Patients who develop cardiovascular complications, among them 96% were hypertensive, followed by 46.8% diabetic & 42.1% smoker (Graph 1).

Over one quarter (28.6%) patients had family history of DM & the rest 17.5 had of HTN. Echo findings show 70% patients had concentric hypertrophy & 30% Eccentric Hypertrophy. Male & Female both had mean Left Ventricular Mass Index (LVMI) higher than normal limit. The mean inter ventricular sepal thickness (IVST) & Posterior Wall Thickness (PWT) were also above the normal limit. However, LVID in both systole & diastole were with in normal limit.

The mean Hb level was significantly less among those, who developed cardiovascular complication than who did not develop the same (P=0.014). Blood sugar 2 hrs after breakfast, Blood urea, Serum k^+ & S. creatinine were significantly higher among those who developed cardiovascular complications compare to those who did not developed the same complications (Table 2).

Table 2: Comparison of biochemical variables between groups

Biochemical variables #	Cardiovascular complications developed		P-value*
	Yes (n = 77)	No (n = 49)	
Haemoglobin (gm/dl)	8.6 ± 1.5	11.1 ± 4.5	0.014
Blood sugar 2 hours after breakfast (mmol/L)	9.2 ± 1.6	7.1 ± 1.7	< 0.001
Blood urea (mmol/L)	27.4 ± 3.1	20.0 ± 6.2	< 0.001
Serum creatinine (mg/ dl)	11.1 ± 1.7	9.0 ± 2.7	< 0.001
Serum Na^+ (meqv/L)	141.5 ± 8.8	139.5 ± 4.0	0.123
Serum K^+ (meqv/L)	5.9 ± .6	5.3 ± 0.73	< 0.001
Serum Ca^+ (mg/dl)	6.3 ± 2.4	8.4 ± 2.2	< 0.001

*Student's t-Test was used to analyse the data and presented as mean ± SD

Table 3 compares the comorbidites between groups. All the comorbidites Hypertension, Diabetes, smoking, family history of HTN and family history of Diabetes was observed to be significantly higher among patients associated with cardiovascular complications (p = 0.022, p < 0.001, p = 0.005, p < 0.001 and p = 0.007 respectively).

Table 3: Comorbidites in ESRD patients with or without cardiovascular complications

Comorbidites	Cardiovascular complications developed		P-value
	Yes (n = 77)	No (n = 49)	
Hypertension#			
Present	74(96.1)	37(75.5)	0.022
Absent	3(3.9)	12(24.5)	
Diabetes*			
Present	58(75.3)	1(2.0)	< 0.001
Absent	19(24.7)	48(98.0)	
Smoking habit#			
Present	40(51.9)	13(26.5)	0.005
Absent	37(48.1)	36(73.5)	
Family history of DM*			
Present	35(45.5)	1(2.0)	< 0.001
Absent	42(54.5)	48(98.0)	
Family history of HTN*			
Present	19(24.7)	3(6.1)	0.007
Absent	58(75.3)	46(93.9)	

X^2 Tests was conducted to analyse the data. *Fisher's Exact Test was employed to analyse the data. Figures in the parentheses denote corresponding percentage

Discussion

The present study evaluated 126 ESRD patients on MHD. Out of 126 patients, 77(61.1%) developed Cardiovascular complications. In another study on 117 patients on MHD 60% developed Cardiovascular disease.[13] More than 80% of patients

in Cardiovascular complications group were ≥ 50 yrs of age but among those who did not develop cardiovascular complications only 30.6% were above 50 years (P=0.001).

It shows Cardiovascular complications more common in older of patients. Benedetto & co-works also showed that, development of cardiovascular complications in patients of ESRD was significantly associate with advancing age.[2]

HTN, DM, smoking, family history of HTN & DM were significantly higher in patients with Cardiovascular complications than those without (P<0.05). Another study found Diabetes & HTN as risk factors for cardiovascular complications in patients of ESRD on MHD.[14] Other study also showed that, development of Cardiovascular complications in patients of ESRD was significantly associated with diabetes than that with non-diabetic population.[2] From the present study as well as others study suggests that, Diabetic patients have more chance of developing cardiovascular complications in CKD.

HTN is almost universal in patients suffering from severe degree of Renal Failure.[15] HTN in ESRD patients is mostly due to salt & fluid over load & BP can be controlled by adequate HD. However, whether BP is an important predictor of Cardiovascular morbidity & mortality in dialysis patient is still a detectable issue. In a recent retrospective study of 184 non Diabetic patients with CKD suffering uncontrolled BP > 140/90, they showed high Blood Pressure as an independent risk factor for all, cause mortality & the main risk factor for Cardiovascular mortality.[16] Besides HTN & Anemia, recent studies suggest that uremia leads to complications of cardiovascular system.[17]

A prospective observational study conducted on 150 Diabetic ESRD patients on haemodialysis showed that better Glycaemic control was associated with longer survival.[7] Another study found Diabetes & HTN as risk factors for cardiovascular complications in patients of ESRD on MHD.[15]

In this study the different types of cardiovascular complications were LVF 63.6%, IHD 23.4%, CCF 10.4% & Cardiomyopathy 2.6%. Left Ventricular Hypertrophy (LVH) was due to uncontrolled HTN & Chronic Severe Anemia.

In present study, 23.4% had Ischemic Heart Disease (IHD). It's high prevalence due to poor control of BP, anaemia & other risk factor. IHD is common in ESRD on MHD and common cause for mortality.[18]

CCF is common in patients of ESRD on MHD is major risk factor for Cardiac mortality. 10.4% of our patients had CCF. The high prevalence of CCF may be explained by poor control of Blood Pressure, Chronic Severe Anaemia & fluid overload, inadequate Dialysis & Ultrafiltration. Only 2.6% had Cardiomyopathy.

In our study, HTN, DM, smoking, family history of HTN, DM, Obesity were significantly higher in the cardiovascular complication group than those in who no complication have (P=<0.01).

In the present study, biochemical parameters like low Hb, high Blood Sugar, S. Creatinine and S. Potassium were significantly higher in patients who develop Cardiovascular Complications. Control of Blood Pressure, keeping Hb at normal range & good Glycaemic control all these three factors are higher in ESRD patients on MHD, who develop Cardiovascular Complications. Further well designed studies are needed to exactly identify the risk factors for Cardiovascular Complications.

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Prevention and control of rheumatic heart disease among school aged children (5-15 years) in a rural area of Bangladesh

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The ORION Medical Journal 2010 May;33(2):742-744

Abstract

This is a prospective, monocentric, clinical research work conducted in a rural community based health care centre, Chatkhil, Noakhali for the period of one Year, July 1, 2007 to June 30, 2008. The prime objective of this work is to study the prevalence of Rheumatic Heart Disease in rural Bangladeshi perspective: together with to evaluate various cardiac lesions in RHD which occurs as complications of RF. Total subjects were 105, where Male 31 (29.52%) & Female 74 (70.47%) cases.

Out of 105 cases, maximum (51 cases, 48.57%) were of 14-15 years age group. Second affected age group was 11-13 years (32 cases, 30.47%). Regarding clinical presentations, Tachycardia was found in 79 (75.23%) and Cardiac murmur in 77 (73.33%) cases. Among Valvular lesions Mitral Valve in mostly affected (48 cases, 45.71%). Second affected valve is Aortic (34 cases, 32.38%). Other valvular & non specific changes of Carditis were also observed. With proper management 79 cases (75.23%) showed satisfactory improvement. RHD occurring as a sequele of RF, a fatal, disabling & life threatening condition invites early & late prophylactic management to save Cardiac Valves from long term damage.

Key words

Rheumatic fever (RF), Rheumatic heart disease (RHD), Prevention, Control.

Introduction

Rheumatic heart disease (RHD) is a common form of heart disease & one of the most important cardiovascular causes of death among children and young adults all over the world.[1] It is estimated that over 6 million children are affected by this disease. RHD accounts for 33 to 50 percent of all cardiac cases both in-patients and out-patients throughout the country.[2]

Streptococcal infection is very common in children living in under-privileged children and rheumatic fever is reported to occur in 1-3% of those conditions.[3,4]

Rheumatic Heart Disease (RHD) is a very disabling and life threatening condition.[5] It is worsen gradually. Cardiac valve involvement and damage make the patients life criffled. But proper management of Rheumatic Fever & its sequele RHD with Penicillin and other medications can stop this violent disaster to many instances.

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Materials and methods

This study was carried out on 105 human subjects, age limit 5-15 years, no sex variation. All patients were included in the study after obtaining consent from them or their relatives.

Cases clinically diagnosed as RHD were manifested by multiple big joints pain/swelling, chest pain, palpitation, tachycardia, cardiac murmurs (carditis) were selected for Blood- CP, ASO, Anti-streptokinase, Anti-streptozyme (ASTZ), Anti - DNAse-B, Throat swab C/S, Chest x-ray P/A, ECG and Echocardiography to detect valvular lesions.

Human Latex particles reagents were used for serological tests where as ECG was done by FUKUDA DENSHI FX-7102 and Echocardiography by ALOKA-SSD 1100 equipments.

Aims and objectives

1. To study the prevalence of RHD is rural Bangladeshi perspective.
2. To find out the age & sex distribution of patients.
3. To study the various criteria of rheumatic heart disease.
4. To evaluate various cardiac lesions especially valvular lesions.
5. Finally to study the long term outcome of treatment in RHD cases.

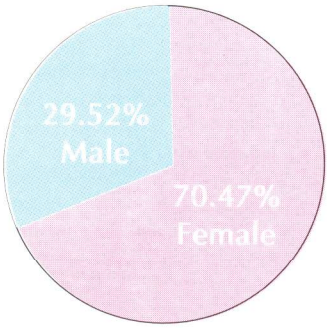
Results

Data were collected from all patients very carefully. Results obtained from the study were narrated in tabulated forms. statistical analysis was done to find out the 'P' value.

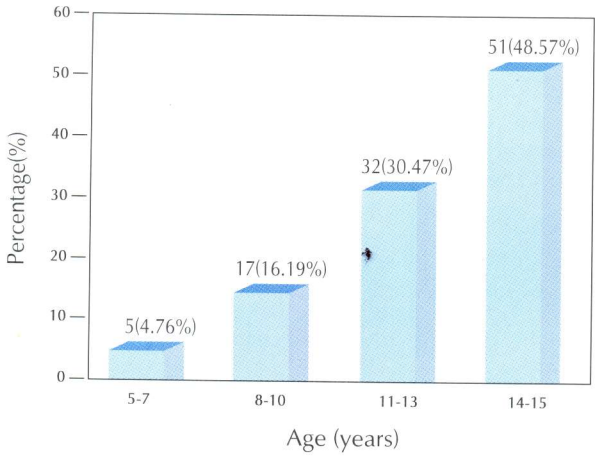
Table 1: Revised Jone's criteria for diagnosis of rheumatic fever

Major criteria	Minor criteria
Arthritis	Fever
Carditis	Arthralgia
Chorea	Raised ESR
Subcutaneous nodule	Raised CRP
Erythema marginatum	1^0 HB, ASO +ve

Two major or one major plus two minor criterias with recent h/o sore throat, pharyngo- tonsillitis or positive throat swab, h/o scarlet fever indicates rheumatic fever.



Graph 1 : Pie- diagram showing gender distribution of RHD cases (n= 105)



Graph 2: Bar-diagram showing age distribution of RHD cases (n= 105)

Table 2 : Clinical Presentations of RHD Positive Cases (n=105)

Clinical presentation	Number	Percent
Polyarthritis or arthralgia	105	100
Chest pain	43	40.95
Shortness of breath	41	39.04
Tachycardia	79	75.23
Cardiac murmur	77	73.33

Table 3 : Investigation reports in RHD cases (n= 105)

Test	Number	Percent
Raised ESR	76	72.38
Positive ASO	80	76.19
Raised CRP	69	65.71
Positive Throat swab	65	61.90
ECG: 1^0 HB, Tachycardia ST changes	81	77.14
Echo: Raised EPSS Valve lesions Chamber dilatations	83	79.04

Table 4 : Valvular lesions in RHD cases (n= 105)

Valves involved	Number	Percent
❑ MV (MR/MS/Valvulitis)	48	45.71
❑ MV+AV(MSR ASR)	34	32.38
❑ MV+AV+TV	8	7.61
❑ AV (AS/AR alone)	5	4.76
❑ Carditis + other non-specific ST-T changes	10	9.52

Table 5 : Bed rest plus ambulation time for RHD cases

Cardiac status	Management
A. No Carditis	Bed rest - 2 weeks, and Gradual ambulation-2 weeks
B. Carditis	Bed rest- 4 weeks, and Gradual ambulation-4 weeks
C. Carditis and Cardiomegaly	Bed rest- 6 weeks, and Gradual ambulation-6 weeks
D. Cardiomegaly and Heart Failure	Bed rest- 8 weeks, and Gradual ambulation-8 weeks

Table 6 : Drug therapy for RF & RHD

Clinical manifestations	Treatment
Arthralgia	Analgesics only
Arthritis	Aspirin-100 mg/kg/day for 2 weeks and 75 mg/kg/day for 4-6 weeks.
Carditis	Prednisolone-2mg/kg/day for 2 weeks, taper of 2 weeks. Aspirin 75 mg/kg/day at 2 weeks and continue for 6 weeks.

Table 7 : Primary prophylaxis for RF & RHD

Drug	Mode	Dose
Benzathine Penicillin	IM	i)12 lac for adult & children> 30 kgs ii) 9 lac for 25-30 kgs iii) 6 lac for <25 kgs
Phenoxymethyl Penicillin	Oral	i) 250 mg 6 hourly for adult & children over 25 kgs ii) 125 mg 6 hourly children < 25 kgs for 10 days
For Penicillin sensitive Erythromycin	Oral	i) 250 mg 6 hourly for adults & children over 25 kgs ii) 40mg/kg/day for children < 25 kgs

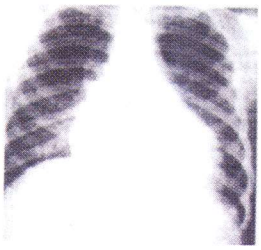


Figure: 1 Cardiomegaly due to RHD

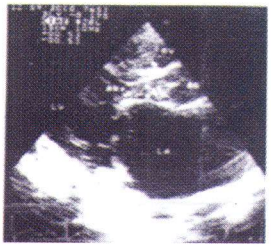
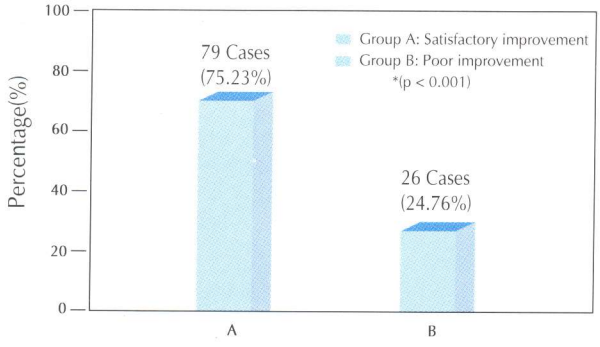


Figure: 2 Echo MR in RHD

Table 8 : Secondary prophylaxis for RF & RHD

Mode	Drug	Dose
IM	Benzathine Penicillin	12 lac 4 weekly (adult) 6 lac 4 weekly (children < 25 kgs)
Oral	Phenoxymethyl Penicillin	250 mg bd (adult) 125 mg bd (children)
Oral	Erythromycin	250 mg bd (adult) 125 mg bd (children)



Graph 3: Bar-diagram showing outcome of treatment

Discussion

Diagnosis of RF & RHD is not very easy. Multiple clinical presentations are associated with RF. Although it is a multi system involvement disease, Revised Jone's criteria is accepted by American Heart Association (AHA) as initial guidelines for diagnosis of RF which is shown in table 1.[6]

Graph 1 exhibits the gender distribution of patients where male 31 (29.52%) and female 74 cases (70.49%). In our study, girls are affected more, which is consistent with the findings of Ibarnagary and co-workers in 1999.[7]

Among 105 RHD cases, age distribution is tabulated in Graph 2, which exhibits peak incidence (51 cases, 48.57%) in 14-15 years age group. Second affected group is 11-13 years (32 cases, 30.47%). These findings have got similarity with those of Portillis & co-workers in Argentina in 2004, where 14-15 years group: 46.23% and 11-13 years group: 28.59% affected.[8]

Various clinical presentations are narrated in Table 2. All patients had polyarthritis or arthralgia. Tachycardia was seen in 79 cases (75.23%) and cardiac murmur in 77 cases (72.33%).

Investigation reports were tabulated in Table 4. Routine Haematological and Serological tests together with ECG & Echocardiography were performed. Among those ECG changes were seen in 81 (77.14%), echo changes in 83 (79.04%) and positive ASO in 80 cases (76.19%) respectively. These findings are consistent with those of Malhamza and Pathania in 2006, where ECG-80.72%, ECHO-76.24%, ASO-75.29% positivity and sensitivity in RHD cases.[9]

Multivalvular lesions are seen in RHD among which Mitral valve is mostly affected (48 cases, 45.71%). Next affected valve is Aortic (34 cases, 32.38%). Sugohata and other researchers also found almost same results 47.22% for Mitral & 34.77% for aortic valve respectively.[10]

Though disease process is very notorious in RF & RHD, we have observed satisfactory improvement in 79 cases (75.23%) with primary and secondary prophylaxis, which is supported by research workers of European Heart Association having success rate almost 76.98%).[11]

Conclusion

Bangladesh, a developing third world country is not free from RF & RHD. Diagnosis is not very easy though simple positive ASO in not a major criteria for diagnosis of RF. Here should be no place for over diagnosis or under diagnosis. Proper management of RF & RHD can save millions of lives through out the world per year.

Acknowledgement

This research work was conducted with the compliments of Ministry of Science, Information and Communication Technology, Govt. of Bangladesh, but neither influencing the findings of this research work, nor its contents for publication.

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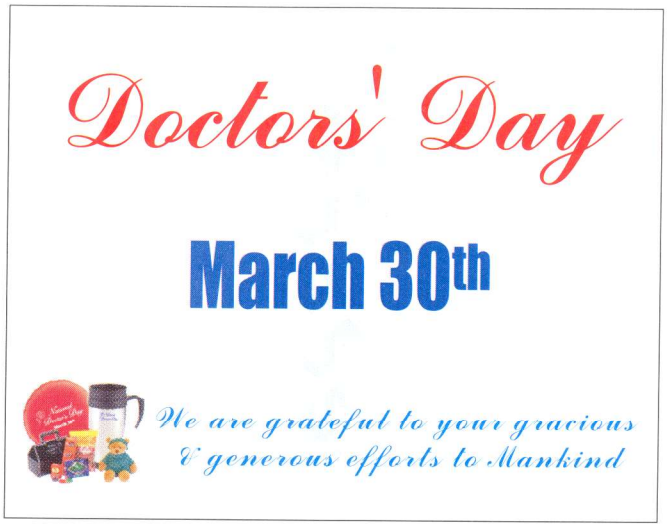
Medi Clip

A brief history of Doctors' Day

This first observance included the mailing of cards to the physicians and their wives, flowers placed on graves of deceased doctors, including Dr. Long, and a formal dinner in the home of Dr. and Mrs. William T. Randolph. After the Barrow County Alliance adopted Mrs. Almond's resolution to pay tribute to the doctors, the plan was presented to the Georgia State Medical Alliance in 1933 by Mrs. E. R. Harris of Winder, president of the Barrow County Alliance. On May 10, 1934, the resolution was adopted at the annual state meeting in Augusta, Georgia. The resolution was introduced to the Women's Alliance of the Southern Medical Association at its 29th annual meeting held in St. Louis, Missouri, November 19-22, 1935, by the Alliance president, Mrs. J. Bonar White. Since then, Doctors' Day has become an integral part of and synonymous with, the Southern Medical Association Alliance. Through the years the red carnation has been used as the symbol of Doctors' Day.

By the above sequence, on March 30, 1958, a Resolution Commemorating Doctors Day was adopted by the United States House of Representatives. In 1990, legislation was introduced in the House and Senate to establish a Doctors Day. Following overwhelming approval by the United States Senate and the House of Representatives, on October 30, 1990, President of U. S. signed S.J. RES. #366 (which became Public Law 101-473) designating March 30 as "Doctors Day."

doctorsday.org



An overview and update management of myelodysplastic syndrome

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The ORION Medical Journal 2010 May;33(2):745-747

Abstract

The myelodysplastic syndromes (MDS) are clonal disorders of haemopoiesis. They share characteristic morphological abnormalities of the blood and bone marrow. The majority of patients are elderly and present with symptoms of marrow failure despite increased marrow cellularity.

Epidemiology

MDS appears to be the most common malignancy world-wide specially among the elderly and the risk of developing MDS increases dramatically with age.

Table: 1 Overall annual incidence 3-4/100,000 population.

Age (yrs)	incidence (per 100,000 population)
<50	0.5
50-59	5.3
60-69	15
70-79	49
>80	89

The median age of developing MDS is 65 years with a slight male predominance (Male : Female =1.4:1).

Etiology and predisposing factors

Patients are described as having Primary MDS (De novo), when no cause is apparent and having Secondary/ Acquired/ Therapy related (TR-MDS), when prior exposure to chemotherapy has occurred. The etiology of most cases of MDS remains unknown but there are some associations.

Heritable predisposition

A. Constitutional genetic disorders

1. Down Syndrome
2. Trisomy 8 mosaicism
3. Familial Monosomy[7]

B. DNA repair deficiencies

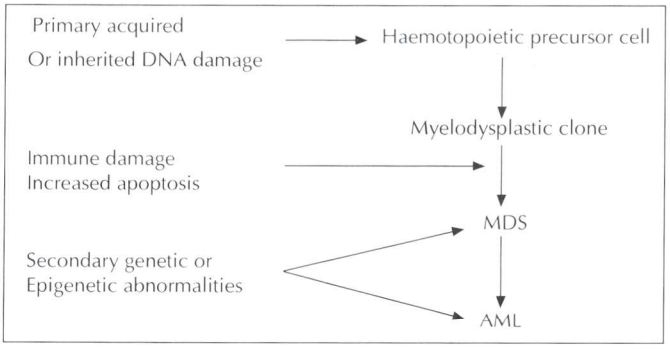
1. Fanconi's Anaemia
2. Ataxia Telangiectasia
3. Bloom Syndrome
4. Xeroderma Pigmentosum

Acquired predisposition

1. Environmental or occupational exposure to benzene, pesticides, hair dies etc,
2. Tobacco,
3. Paroxysmal Nocturnal Haemoglobinuria,
4. Cytotoxic Therapy with-Alkylating agents, Nitrosoureas, Procarbazine and
5. Autologus Bone marrow transplantation.

Pathogenesis

Factors that contribute to the development of MDS are Heterogenous. Genetic, Functional abnormalities of haematopoietic stem cells, Immunological abnormalities and increased apoptosis of bone marrow cell due to ineffective haematopoiesis play the major role.



Clinical presentation

The majority of patients present with features of bone marrow failure-fatigue, weakness, exercise intolerance, dizziness as a result of undiagnosed Anemia.

Less commonly patients present with frequent infections, easy bruising or bleeding.

A few patients are diagnosed incidentally during the routine investigation.

There are also some rare associations of other diseases which may accompany MDS such as auto-immune diseases: cutaneous vasculitis, mono-articular arthritis, pericarditis, pleural effusion, skin ulcerations, iritis myositis, peripheral neuropathy, sweet syndrome granulocytic sarcoma.

Laboratory findings

Unexplained anaemia, leukopenia and thrombocytopenia with or without monocytosis and a hypercellular marrow with dysplstic cell morphology-is the classical heamatological findings in a patient of MDS.

PBF & Bone marrow findings

Lineage	Peripheral Blood	Bone Marrow
	Anaemia- majority of cases, Pancytopenia-30-50%, 20% have Anaemia + Neutropenia or Thrombocytopenia Less commonly, isolated thrombocytopenia or isolated leukopenia may be found.	Hypercellular (hypocellular in 20% cases).
Erythroid	Ovalmacrocytosis anisopoikiloctosis, nRBC, basophillic stippling.	Megaloblastoid erythropoiesis, Nuclear budding, Ringed Sideroblasts, Inter-nuclear bridging, dyskaryorrhexis , nuclear fragments, cytoplasmic vacculization, multinucleation.

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	Peripheral Blood	Bone Marrow
Myeloid	Pelger- Huet anomaly, Hypogranulation, Hypersegmentation, Ring shaped nuclei.	Defective granulation, Maturation arrest at myelocyte stage, Increased blast.
Megakaryocytes	Giant platelets, Hypogranular or Agranular platelets.	Micromegakaryocytes, Large mono-or-binuclear magakaryocytes.

It should be kept in mind that, dysplastic morphology may also be seen in healthy elderly indivisuals (affecting <10% of marrow cells) & in a varity of non-clonal disorders including:

- Vit-B_{12} & Folate deficiency.
- Heavy metal & Alcohol poisoning.
- HIV infection.
- Treatment with anti-TB drugs.

Diagnosis of MDS is difficult when dysplastic features are obscure. In these cases, special investigations are needed for proper diagnosis. They are as follows:

- Cytogenetic Analysis.
- Trephine Biopsy.
- Flow Cytometry.
- Immuno-histochemical Studies.

Differential diagnosis

- Megalobioystic anemia
- Erythro-Leukaemia (AML-M6)

Management

The management of MDS is generally unsatisfactory.

Observation only

Supportive care with:

I. Red cell & platelet transfusions.
II. Growth factors: Erythropoietin, G-CSF etc.
III. Immunosuppression : Cyclosporine A, Anti - Thymocyte Globulin (ATG), Anti- Lymphocyte Globulin.

- Cytotoxic drugs: Cytaradine, Etoposide, Idarubicin, Fludrarabine.
- New therapies:
  1. Anti - Angiogenic therapy : Thalidomide & its analogue.
  2. Demethylation agents : 5 - Azacytidine & Decitabine.
  3. Arsenic trioxide.
- Transplantation (Stem cell/Allogenic/Autologus): Only curative treatment.

Theraputic strategy

Low risk MDS group (IPSS low)

- Close monitoring at patients for disease progression.
- Supporative care for symptomatic relief of anaemia, thrombocytopenia and infection due to neutropenia (Red cell & Platelet transfusions, Growth Factors: Erythropoietin, G-CSF etc.).
- Immunosuppression with Cyclosporine A.
- Anti-Angiogenic Therapy with Thalidomide & its analogue.

Intermediate-1 risk MDS group

- If Patient's Age < 50 yrs & short disease duration- Treatment of choice is Stem Cell Transplantation.
- Other treatmient Options- Same as for the low risk group.

Intermediate-2 / high risk MDS group

- Chemotherapy- either single Cytarabine / Idarubicin or in combination Etoposide + Fludarabine, Topotecan + Cytarabine.
- After Chemo if there is "Complete Remission", Pt's age <65yrs- Allogenic/Stem Cell Transplantation can be considered.

Clinical course

The course of MDS is variable.

- Stable course over many years.
- Gradual increase in the % of marrow blasts.
- Rapid increase in the blast cells.
  -10-40% patients develop AML
  -20-40% patients die of infection or bleeding or both
  -Marrow failure
  -Secondary myelofibrosis

Prognosis

As the MDS display remarkable clinical, pathologic & cytogenetic heterogenicity, it is necessary to scrutiny the prognostic factors carefully to optimize treatment decisions.

Some adverse prognostic factors

Increasing age, therapy related MDS, severe cytopenias, increased blasts, trilineage dysplasia, complex chromosomal abnormalities, karyotypic evolution, P_{53} & RAS mutations, P_{15} hypermethylation, telomere shortening, CD7-positive blasts.

Recently adopted "the International Prognostic Scoring System" (IPSS) takes blast percentages, cytogenetic abnormalities & the number of cytopenic cell lines into consideration.

Score values	0	0.5	1.0	1.5	2.0
Marrow blasts (%)	<5	5-10	-	11-20	21-30
Karyotype*	good	intermediate	poor	-	-
Cytopenias**	0/1	2/3	-	-	-

*Good-normal, -Y, del (5q), del(20q), Poor: complex($\geq$ 3 abnormalities) or chromosome 7 anomaly. Intermediate = other abnormalities. Cytopenias defined as **Hb<10/g/dl, Platelets <$100x10^9$/1, neutrophils<$1.5x10^9$/1.

Table: 2 Median survival of primary MDS using the IPPS Score

Risk group	Score	Median survival			
		< 60yrs	> 60yrs	<70yrs	> 70yrs
Low risk group	0	11.8	4.8	9	3.9
Intermediate-1 risk group	0.5-1.0	5.2	2.7	4.4	2.4
Intermediate-2 risk group	1.5-2.0	1.8	1.1	1.3	1.2
High risk group	>2.5	0.3	0.5	0.4	0.4

Conclusion

The discovery of novel agents such as Anti-angiogenic therapy like Thalidomide and its analogue (Revimid) is essential for prolonging the survival of this group of patients. Physicians should refer their patient in specialized centre for clinical trials involving these novel therapies under the guidance of Haemato-oncologists.

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MSD News

Medical Services Department (MSD) of ORION Laboratories Ltd. successfully arranged number of Scientific Seminar & Round Table Meeting in different venues of all over Bangladesh during December 2009 to April 2010.

Scientific Seminar (SS)

Comilla

Medicine Unit, CoMCH: On 13th December 2009 Medicine Department of Comilla Medical College Hospital arranged a scientific seminar on "Iron Deficiency Anemia & Its Management" in Capsicum restaurant. Dr. Shahab Uddin, Head of the Department of Medicine of Comilla Medical College Hospital adorned the seat of Chairperson.

Obs & Gynae Unit, CoMCH: A scientific seminar on "Iron Deficiency Anemia & Its Management" was arranged by the Obs & Gynae Department of Comilla Medical College Hospital on 10th January 2010 in Capsicum restaurant. Dr. Golam Anwar Khan, Head of the Department of Obs & Gynea chaired the seat of Chairperson.

Medicine Unit, CoMCH: Medicine Department of Comilla Medical College Hospital arranged a scientific seminar on "Gastro Intestinal Bleeding & Its Prevention" in Capsicum restaurant on 10th April 2010. Dr. Shahab Uddin, Head of the Department of Medicine of Comilla Medical College Hospital adorned the seat of Chairperson.

Round Table Meeting (RTM)

Dhaka

Hepatology Department, BSMMU: Hepatology Department of BSMMU arranged a round table meeting on 23rd February 2010 on "Gastro Intestinal Bleeding & Its Prevention" at China Kitchen Chinese Restaurant. Dr. Fakruddin Ahmed, Consultant of Hepatology Department of BSMMU, adorned the seat of Chairperson.

Neurosurgery Department, BSMMU: A round table meeting was arranged by the Neurosurgery Department of BSMMU on 21st March 2010, on "Omeprazole in NSAID Induced Ulcer Prophylaxis" at China Kitchen Chinese Restaurant. Associate Professor of Neurosurgery Department of BSMMU, Dr. Samsul Alam adorned the seat of Chairperson of the meeting.

Surgery Department, BSMMU: A round table meeting was arranged by the Surgery Department of BSMMU on 25th April 2010, on "Omeprazole in NSAID Induced Ulcer Prophylaxis" at China Kitchen Chinese Restaurant. Associate Professor of Surgery Department of BSMMU, Dr. Shahidur Rahman adorned the seat of Chairperson of the meeting.

DNMCH: Medicine Unit-2 of Dhaka National Medical College Hospital, on 9th February 2010, arranged a round table meeting on "Gastro Intestinal Bleeding & Its Prevention". Dr. A. K. M. Morshed, Associate Professor & Head of MU-2 of DNMCH was adorned the seat of Chairperson.

Sreenagar THC: A round table meeting arranged by the Sreenagar THC on 25th January 2010 on "Gastric Acid Related Disorder". Dr. Kazi Shariful Alam, THA was chaired the seat of the Chairperson.

Mymensing

MMCH, Mymensing: A round table meeting was arranged by the Pediatrics Department of Mymensing Medical College Hospital on "Early Childhood Development & Role of Ceftazidime in Neonate Infection" on 23rd February 2010 in MMCH seminar room. Prof. (Dr.) Azizul Hoque, Head of Pediatric Department adorned the seat of Chairperson.

Barisal

SBMCH, Barisal: Medicine Unit -1 of Sher-E-Bangla Medical College Hospital, Barisal arranged a round table meeting on "Iron Deficiency Anemia & Its Management" on 16th March 2010 in SBMCH MU-1. Dr. Emrul Kayesh, IMO of MU-1 adorned the Chairperson's seat.

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Multiple myeloma: A review

Sarker HN[1], Saha B[2], Das BP[3]

The ORION Medical Journal 2010 May;33(2):748-751

Abstract

Multiple Myeloma (Myelo from bone marrow), also known as MM, Myeloma, plasma cell myeloma, or as Kahler's disease (after Otto Kahler) is a malignant proliferation of plasma cells. These Immune cells are formed in bone marrow, are numerous in lymphatics and produce antibodies. Myeloma is incurable, but remissions may be induced with Steroids,Chemotherapy, Thalidomide and stem cell transplants. Median survival is 3 years, but the introduction of novel treatments in the last decade have improved this prognosis to 50-55 months.[1] Chromosome diagnosis can separate patients into more or less favorable prognoses. Myeloma is part of the broad group of diseases called hematological malignancies.

Epidemiology

The incidence of myeloma is 4/100000 new cases per annum,[2] with a Male:Female ratio of 2:1. The median age of diagnosis is 60-70 years and the disease is more common in Afro-Caribbeans.

Multiple myeloma is the second most prevalent blood cancer (10%) after Non-Hodgkin's lymphoma.[3] It represents approximately 1% of all cancers and 2% of all cancer deaths. Although, the peak age of onset of multiple myeloma is 60 to 70 years of age, recent statistics indicate both increasing incidence and earlier age of onset.

African Americans and Native Pacific Islanders have the highest reported incidence of this disease in the United States and Asians the lowest. Results of a recent study found the incidence of myeloma to be 9.5 cases per 100,000 African Americans and 4.1 cases per 100,000 Caucasian Americans. Among African Americans, myeloma is one of the top 10 leading causes of cancer death.

Pathophysiology

Normal plasma cells are derived from B-cells and produce immunoglobulins, which contain heavy and light chains. Normal immunoglobulins are polyclonal, which means that a variety of heavy chains are produced and each may be of kappa or lambda light chain type. Multiple myeloma develops in post-germinal center B lymphocytes. The normal cell line most closely associated with MM cells is generally taken to be either an activated memory B cell or the precursor to plasma cells, the plasmablast.[4]

In myeloma, plasma cells produce Immunoglobulin of a single heavy and light chain, a monoclonal protein commonly referred to as a paraprotein. In some cases, only light chain is produced and this appears in the urine as Bence Jones proteinuria. Two types in myeloma is shown below.

Type of paraprotein	Relative frequency (%)
IgG	55
IgA	21
Light chain only	22
Others (D, E, non-secretory)	2

A chromosomal translocation between the immunoglobulin heavy chain gene (on the fourteenth chromosome, locus 14q32) and an oncogene (often 11q13, 4p16.3, 6p21, 16q23 and 20q11) is frequently observed in patients with multiple myeloma.[5] This mutation results in dysregulation of the oncogene, which is thought to be an important initiating event in the pathogenesis of myeloma.

The result is proliferation of a plasma cell clone and genomic instability, that leads to further mutations and translocations. The chromosome 14 abnormality is observed in about 50% of all cases of myeloma. Deletion of (parts of) the thirteenth chromosome is also observed in about 50% of cases.

Although, a small number of malignant plasma cells are present in the circulation, the majority are present in the bone marrow. The malignant plasma cells produce Cytokines (especially IL-6), which stimulate Osteoclasts and result in net bone absorption. The resulting lytic lesions cause bone pain, fractures and Hypercalcaemia. Marrow involvement can result in Anaemia or Pancytopenia.

The produced antibodies are deposited in various organs, leading to renal failure, polyneuropathy and various other myeloma-associated symptoms.

Sign and symptom

Because many organs can be affected by Myeloma, the symptoms and signs vary greatly. A mnemonic sometimes used to remember the common tetrad of multiple myeloma is CRAB: C = Calcium (elevated), R = Renal failure, A = Anemia, B = Bone lesions.[6] Myeloma has many possible symptoms, and all symptoms may be due to other causes. They are presented here in decreasing order of incidence.

Bone pain

Myeloma bone pain usually involves the spine and ribs, and worsen with activity. Persistent localized pain may indicate a pathological bone fracture. Involvement of the vertebrae may lead to spinal cord compression. These bone lesions are lytic in nature and are best seen in plain radiographs, which may show "Punched-Out" resorptive lesions (including the "Pepper Pot" appearance of the skull on radiography). The breakdown of bone also leads to release of calcium into the blood, leading to hypercalcemia and its associated symptoms (polyurea, polydipsea and tiredness)

Infection

The most common infections are Pneumonias and Pyelonephritis. Common Pneumonia pathogens include *S. pneumoniae, S. aureus, and K. pneumoniae,* while common

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pathogens causing Pyelonephritis include *E. coli* and other gram-negative organisms. The greatest risk period for the occurrence of infection is in the initial few months after the start of Chemotherapy.[7] The increased risk of infection is due to immune deficiency resulting from diffuse Hypogammaglobulinemia, which is due to decreased production and increased destruction of normal antibodies. A selected group of patients may benefit from replacement Immunoglobulin therapy to reduce the risk of infection.[8]

Renal failure

Renal failure may develop both acutely and chronically. It is commonly due to hypercalcemia (see above). It may also be due to tubular damage from excretion of light chains, also called Bence Jones proteins, which can manifest as the Fanconi syndrome (Type 2 renal tubular acidosis). Other causes include glomerular deposition of Amyloid, Hyperuricemia, recurrent infections (Pyelonephritis), and local infiltration of tumor cells.

Anemia

The Anemia found in Myeloma is usually normocytic and normochromic. It results from the replacement of normal bone marrow by infiltrating tumor cells and inhibition of normal red blood cell production (Hematopoiesis) by Cytokines.

Neurological symptoms

Common problems are weakness, confusion and fatigue due to hypercalcemia. Headache, visual changes and retinopathy may be the result of hyperviscosity of the blood depending on the properties of the paraprotein. Finally, there may be radicular pain, loss of bowel or bladder control (due to involvement of Spinal Cord leading to Cord Compression) or Carpal Tunnel Syndrome and other Neuropathies (due to infiltration of peripheral nerves by Amyloid). It may give rise to Paraplegia in late presenting cases.

Diagnosis

Investigations

The diagnosis of Myeloma requires two of the following criteria:

- Skeletal lesions.
- Serum and/or urinary paraprotein.
- Increased malignant plasma cells in the bone marrow.

Skeletal survey, plasma and urinary electrophoresis and Bone marrow aspiration are thus required.

Workup

Skeletal survey: X-rays of the skull, axial skeleton and proximal long bones.

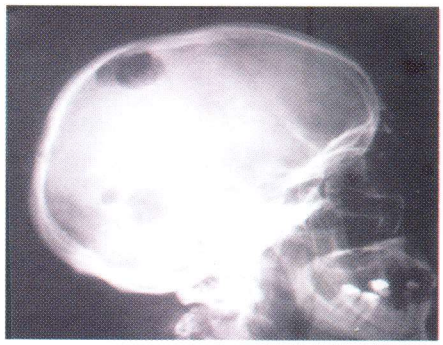

Figure 1: X-rays of the skull

Figure 1 shows lytic lesions (with local disappearance of normal bone due to resorption), and on the skull x-ray as "punched-out lesions.

Magnetic resonance imaging: MRI is more sensitive than simple X-ray in the detection of lytic lesions, and may supersede skeletal survey, especially when vertebral disease is suspected.

CT scan: Performed to measure the size of soft tissue plasmacytomas.

Serum protein electrophoresis: Serum protein electrophoresis showing a paraprotein (peak in the gamma zone) in a patient with multiple myeloma.

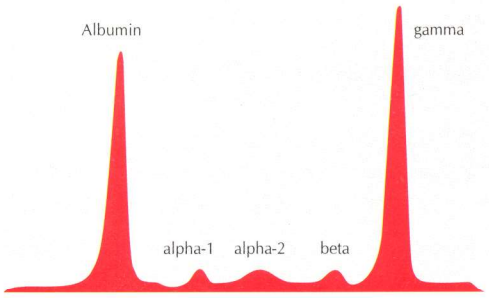

Figure 2: Serum protein electrophoresis

A bone marrow biopsy: Usually performed to estimate the percentage of bone marrow occupied by plasma cells. This percentage is used in the diagnostic criteria for myeloma.

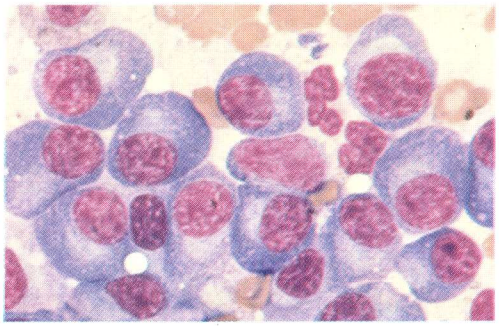

Figure 3: Myeloma cells in bone marrow

Other investigations

- CBC with ESR: ESR is elevated
- PBF: increased rouleaux formation
- Serum calcium: Elevated
- Renal function test: Urea and electrolytes
- Urine for Bence jones protein

Diagnostic criteria

In 2003, the International Myeloma Working Group agreed on diagnostic criteria for symptomatic myeloma, asymptomatic myeloma and MGUS (Monoclonal Gammopathy of Undetermined Significance).[6]

Symptomatic myeloma

1. Clonal plasma cells >10% on bone marrow biopsy or (in any quantity) in a biopsy from other tissues (plasmacytoma).

2. A monoclonal protein (paraprotein) in either serum or urine.
3. Evidence of end-organ damage (related organ or tissue impairment, ROTI):
   - Hypercalcemia (corrected calcium >2.75 mmol/L)
   - Renal insufficiency attributable to myeloma
   - Anemia (hemoglobin <10 g/dl)
   - Bone lesions (lytic lesions or osteoporosis with compression fractures)
   - Frequent severe infections (> 2 a year)
   - Amyloidosis of other organs
   - Hyperviscosity syndrome

Asymptomatic myeloma

1. Serum paraprotein >30 g/L and /or
2. Clonal plasma cells >10% on Bone Marrow biopsy and
3. No myeloma related organ or tissue impairment

Monoclonal gammopathy of undetermined significance (MGUS)

1. Serum paraprotein <30 g/L and
2. Clonal plasma cells <10% on Bone Marrow biopsy and
3. No myeloma related organ or tissue impairment.

Related conditions include solitary plasmacytoma (a single tumor of plasma cells, typically treated with irradiation), plasma cell dyscrasia (where only the antibodies produce symptoms, e.g. AL amyloidosis), and POEMS syndrome Peripheral Neuropathy, Organomegaly, Endocrinopathy, Monoclonal plasma cell disorder, skin changes.

Staging

International staging system: The International Staging System (ISS) for myeloma was published by the International Myeloma Working Group in 2005: [9]

- Stage I: β_2-microglobulin (β_2M) < 3.5 mg/L, albumin ≥ 3.5 g/dl
- Stage II: β_2M < 3.5 and albumin < 3.5; or β_2M ≥ 3.5 and < 5.5
- Stage III: β_2M ≥ 5.5

Treatment

Treatment for Multiple Myeloma is focused on disease containment and suppression.

Asymtomatic multiple myeloma

If the disease is completely asymptomatic (i.e. There is a paraprotein and an abnormal bone marrow population but no end organ damage), treatment may be diferred.

Symptomatic multiple myeloma

Supportive therapy

- High fluid intake to treat renal impairment and hypercalcaemia.
- Analgesia for bone pain.
- Bisphosphonates for hypercalcaemia and to delay other skeletal related events.
- Allopurinol to prevent urate nephropathy.
- Plasmapheresis, as necessary for hyperviscosity.
- Erythropoietin to treat anemia.
- Dialysis for renal failure.

Specific therapy

Initial therapy: Initial treatment of multiple myeloma depends on the patient's age and comorbidities.

■ Under the age of 65 :

A) High dose ablation chemotherapy with hematopoietic stem-cell transplantation.

Autologous stem cell transplantation: The transplantation of a patient's own stem cells after chemotherapy is the most common type of stem cell transplantation for multiple myeloma. It is not curative, but does prolong over all survival.

Allogeneic stem cell transplantation: The transplantation of a healthy person's stem cells into the affected patient, has the potential for a cure, but is only available to a small percentage of patients.[5] Furthermore, there is a 5-10% treatment-associated mortality rate.

B) Alternative therapy: The most common induction regimens used today are thalidomide-dexamethasone, bortezomib based regimen and lenalidomide-dexamethasone.[10]

■ Patients over age 65 :

Patients over age 65 and patients with significant concurrent illness often cannot tolerate stem cell transplantation. For these patients, the standard of care has been chemotherapy with Melphalan 10 mg /m^2 and prednisolone 40 mg / m^2.

Recent studies among this population suggest improved outcomes with new chemotherapy regimens. Treatment with bortezomib, melphalan and prednisone had an estimated overall survival of 83% at 30 months, lenalidomide plus low-dose dexamethasone-an 82% survival at 2 years melphalan, prednisone and lenalidomide had a 90% survival at 2 years. Head to head studies comparing these regimens have not been performed.[11,12]

Relapse

The natural history of myeloma is of relapse following treatment.

Depending on:

a) The patient's condition,

b) The prior treatment modalities used and

c) The duration of remission.

Options for relapsed disease include re-treatment with the original agent (relapse after six months) use of other agents (such as melphalan, cyclophosphamide, thalidomide or dexamethasone, alone or in combination), and a second autologous stem cell transplant (relapse within six months).

Later in the course of the disease, "Treatment Resistance" occurs. This may be a reversible effect, and some new treatment modalities may re-sensitize the tumor to standard therapy.[5]

Chemotherapy

Chemotherapy involves using medicines taken orally as a pill or given through an intravenous (IV) injection, to kill Myeloma cells. Chemotherapy is often given in cycles over a period of months, followed by a rest period. Often Chemotherapy is

discontinued during what is called a plateau phase or remission, during which M protein level remains stable. It may need chemotherapy again if M protein level begins to rise.

Common Chemotherapy drugs used to treat myeloma are Melphalan (Alkeran), Cyclophosphamide (Cytoxan), Vincristine (Oncovin), Doxorubicin (Adriamycin) and Liposomal Doxorubicin (Doxil).

- Corticosteroids: Corticosteroids such as Prednisolone and Dexamethasone have been used for decades to treat Multiple Myeloma. They are typically given as pills. Some research suggests that high doses of steroids may not be needed, and that lower doses may be safer and more effective.

- Stem cell transplantation: This treatment involves using high dose chemotherapy-usually high doses of melphalan -along with transfusion of previously collected immature blood cells (stem cells) to replace diseased or damaged marrow. The stem cells can come from patient or from a donor, and they may be from either blood or bone marrow.

- Thalidomide (Thalomid): Thalidomide, a drug originally used as a sedative and to treat morning sickness in the 1950s, was removed from the market after it was found to cause severe birth defects. However, the drug received approval from the Food and Drug Administration (FDA) again in 1998, first as a treatment for skin lesions caused by leprosy. Thalidomide is currently FDA-approved in conjunction with the corticosteroid called dexamethasone for the treatment of newly diagnosed cases of multiple myeloma. This drug is given orally.

- Bortezomib (Velcade): Velcade was the first approved drug in a new class of medications called proteasome inhibitors. It is administered intravenously. It works by blocking the action of proteasomes, which causes cancer cells to die. One study showed that bortezomib had more than twice the response rate of a commonly used drug, dexamethasone. Bortezomib is approved for use as an initial treatment for people with multiple myeloma.

- Lenalidomide (Revlimid): Lenalidomide is chemically similar to thalidomide, but appears to be more potent and cause fewer side effects. It is given orally. Lenalidomide is FDA-approved for use in combination with dexamethasone as a treatment for people who have received at least one prior therapy for Multiple Myeloma.

- Radiation therapy: This treatment uses high-energy penetrating waves to damage myeloma cells and stop their growth. Radiation therapy may be used to target myeloma cells in a specific area-for instance, to more quickly shrink a tumor that's causing pain or destroying a bone.

Prognosis

The International Staging System can help to predict survival, with a median survival of 62 months for stage-1 disease, 45 months for stage-2 disease, and 29 months for stage-3 diseases.[9]

Poor prognostic features include:

a) High β_2 Microglobulin.
b) Low Albumin.
c) Low Haemoglobin
d) High Calcium at presentation.

Conclusion

Myeloma is incurable, but remissions may be induced with Steroids, Chemotherapy, Thalidomide and Stem cell transplants. Median survival is 3 years, but the introduction of novel treatments in the last decade have improved this prognosis to 50-55 months.[1] There is a great scope for researchers to discover newer drugs to improve survival or cure of Myeloma patients.

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Cough variant asthma

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Introduction

Most clinicians are familiar with cough as a symptom of asthma along with wheezing and breathlessness. However, non-productive cough as the only presenting symptom of asthma is a less often recognized, although well described entity.

Chronic cough has been used to describe a cough that has persisted for more than eight weeks.[1, 2] Non productive cough lasting for more than three weeks but less than eight weeks is often labeled as sub-acute cough which usually resolves spontaneously.[3]

A number of studies have shown cough variant asthma (CVA) to be a leading cause of chronic non-productive cough in both adults and children.[4-14]

CVA was first described by Glauser et al in 1972.[15] After which Carrao et al clearly defined CVA as a variant form of bronchial asthma.[16] CVA has been defined as a chronic persistent non-productive cough more than eight weeks without wheezing,[17] not due to apparent causes and shown bronchial hyperreactivity and relief of coughing following bronchodilator therapy and/or inhaled corticosteroid but little or no response to non-specific anti-tussive agents.[18,19]

Cough variant asthma is sometimes considered as a precursor[16,17,20-22] and also a variant of classic asthma with symptoms of wheezing and dysponea.[16,23] Indeed in up to 6% of asthmatics cough may be the only symptom.[24] Therefore, CVA may be described as an occult form of asthma in which the only sign or symptom is chronic non-productive cough.[25] This common problem amongst all ages frequently goes unrecognized leading to under diagnosis and under treatment.[26] The main reason of under diagnosis or delayed diagnosis in patients with CVA is thought to be absence of wheezing detected by the patients and physicians because wheezing has long been considered the sine quanon of asthma.[27] If this diagnosis is not considered, chronic recurrent cough may be erroneously attributed to chronic bronchitis and ineffectively treated with repeated courses of antibiotics.

'Atopic Cough' although clinically similar to cough variant asthma is a new entity which has some difference from CVA in respect to pathophysiology, diagnosis, treatment and prognosis.[17]

Prevalence

Cough variant asthma, gastro-esophageal reflux (GERD) associated cough and post nasal drip (PNDS) induced cough are well known causes of chronic non-productive cough. Current evidence suggests that CVA may account singly or contribute with other causes in up to 29% of patients referred for specialist treatment of cough.[28] Prevalence of cough variant asthma (CVA) was found among 41.8% of Japanese patients presenting with chronic cough for 8 or more weeks.[28,29] In addition, this disorder accounted for 61% of the patients among the above mentioned population with chronic cough that did not respond to non specific antitussive therapy.[28] But prevalence of CVA in western countries were reported lower, for example 35% by Mc Gravey et al and 25% by Irwin et al.[6,27] This difference might reflect the fact that in western countries GERD and PNDS have been found to be responsible for 10-27% and 29-41% of chronic cough respectively[10,29] while these are very rare in Japanese studies.[30]

Furthermore 'Atopic Cough' as already mentioned a closely related condition to CVA, characterised by chronic non-productive cough has also been claimed to be found in 58% of patients with isolated chronic non-productive cough in some studies.[17]

Pathophysiology

The pathophysiology of chronic cough in asthma has not been clearly elucidated. Some authors have proposed airway bronchoconstriction as the primary cause[31,32,33] while others think that airway epithelial damage leaving exposed vagal cough receptors lead to cough without wheezing.[34,35]

The mechanism of cough in asthma, in view of airflow obstruction has been studied.[36,37] It has been proposed that cough receptors are stimulated by local bronchoconstriction, which is thought to be mediated by mechanosensitive rapidly adaptive receptors.[38] Neural excitement after cough receptors are stimulated is known to be transmitted to the cough centre through two nerve fibres: the medullated A delta fibre and the non-medullated C- fibre.[39,40] The later nerves are crucial in the pathophysiology of cough in CVA and their density has been found higher in CVA patients than in classic asthma.[41]

Mc Fadden[33] described a group of asthmatics for whom cough was the predominant symptom at exacerbation. Pulmonary function tests revealed narrowing of the central airways. Whereas another group of asthmatics who predominantly complained of dysponoea had narrowing of peripheral airways. He attributed the predominance of cough in the former group to central airways obstruction. In a recent study, Mastsumoto has shown that when methacholine is inhaled coughing is more frequent in the CVA group whereas wheezes are more frequent in classic asthma patients.[42] CVA is associated with higher wheezing threshold (the minimal degree of airways obstruction when wheezing become audible) than classic asthma.[43]

Airway sensitivity and reactivity are thought to be differently regulated.[44,45] Analysis of factors related to cough and wheezes revealed that wheezes in classic asthma were associated with airway hypersensitivity and baseline airflow obstruction which in turn is most likely associated with airway inflammation, epithelial damage, abnormal neural control and increased inflammatory cell number and activity. In contrast, airway reactivity is considered most strongly related to smooth muscle

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contractility which is the central feature of CVA.[42] Airway sensitivity is substantially lower in patients with CVA than those in classic asthma.[42]

Pathologically, CVA shares common features such as eosinophilic inflammation and remodeling changes, including sub-basement membrane thickening and goblet-cell hyperplasia with classic asthma.[46-49] Chronic persistent non-productive cough due to other causes such as GERD, PNDS often grouped as non asthmatic chronic cough (NAC) also have some features of airway inflammation and remodeling.[50-52] In a recent study involving CT scan of chest has revealed airway wall thickening in patients with CVA and to a lesser degree in NAC patients compared to normal healthy controls.[53] This is consistent with previous study by endobronchial biopsy showing eosinophilic inflammation and thickening of airway sub-basement membrane in CVA patient.[46,47]

The role of eosinophilic inflammation in classic asthma has already been well established and it has been found that eosinophilic inflammation is involved in CVA as well.[54,55, 56] It has been shown that percentage or number of eosinophils in BAL (Broncho-alvedar lavage) fluid and bronchial tissue and serum ECP (Eosinophilic Cationic Protiein) levels are significantly increased in patients with CVA and classic asthma when compared with controls. Besides serum ECP level and tissue eosinophil number significantly correlate with clinical severity in both conditions.[56] In this respect, `Atopic Asthma' patient show absence of BAL eosinophilia but have bronchial tissue and induced sputum eosinophilia as in CVA.[57-60]

But how inflammation correlates to cough in CVA is not clear. Several review articles speculate on this issue.[61-63] O'conell et al have hypothesised that patients with CVA might have inflammation solely in the large airways where cough receptors are abundant.[24] Warlock[56] has also stated that cough receptors are assumedly stimulated by the inflammation and that cough in CVA is mediated in the central airways by leukotrienes originating from allergic inflammation known to stimulate c-fibre directly.[64,65] This could result in the release of the neuropeptide which elicits activation of mast cells as well as transmission of the excitation to the cough centre, airway contraction and the accentuation of vascular permeability through an axon reflex.[66,67] Participation of tussive mediators such as prostaglandin E_2 and a neuropeptide substance P, which are secreted from eosinophil may also be a possible mechanism of coughing.[54]

Diagnosis

Clinical suspicion, a typical history and subsequent response to bronchodilator therapy are the major points in the diagnosis of cough variant asthma.[3,8,68] The most important aspects of the history is a detailed description of the cough, usually described as persistent and unproductive; it is characteristically nocturnal and may be triggered by exercise, cold air, and upper respiratory tract infection (URTI). There is typically a seasonal variation with worsening of cough during springfall and early winter. As with typical asthma patients, those with cough variant asthma may have positive personal and family history of allergic conditions such as classic asthma, hay fever, eczema, food allergy and allergic rhinitis.[69] In one study, 38% of patients with CVA had a previous history of atopy and in another 64% of children with this diagnosis had positive skin tests.[63,64]

Clinical severity of CVA is classified according to an original scoring system, because no validated severity scores of CVA have been reported. The system takes account not only of the frequency of the symptoms i.e. cough, but of medication required to achieve control, as recommended by Cockrott and Swysun in a recent report on the classification of asthma severity.[66]

Score of 1: Coughing is intermittent (not daily), which can be controlled with an as needed use of an inhaled β_2 agonist alone.

Score of 2: Coughing occurs daily, which can be controlled with a sustained-release theophyline taken twice daily and an inhaled β_2 agonist used as needed.

Score of 3: Coughing occurs daily, which can be partially suppressed but cannot be controlled with a sustained release theophyline taken twice daily and an inhaled β_2 agonist used as needed.

Physical examination is usually normal in cough variant asthma (CVA) patients. By definition, wheezing is absent and although there may be localized ronchi or rales, accessory muscle use is not found.[67] There may be other allergic manifestations apparent on examination or rhinorrhea if the precipitating factor is a URI.

Laboratory and radiographic studies are generally not helpful in the diagnosis. There may be a nasal or peripheral eosinophilia but this is a variable finding.[68,39] Chest X-ray studies are usually normal, as are baseline pulmonary function studies. Decreased PEFR measured during symptomatic periods may be the only abnormal objective finding acutely, but this also is not uniform.[39,67] Although several studies have shown significant direct correlation between airway sensitivity to PEF variability but PEF variability is not a good marker of the degree of airway reactions in patients with CVA.[69-71]

Up to 55% of patients with CVA show positive skin tests to inhalants such as dusts, mold, animal denders and pollen.[64]

A diagnosis of CVA is made when a chronic non-productive cough without wheeze is associated with Airway Hyperresponsiveness (AHR) and a favourable response to asthma therapy in the absence of other discernible causes.[72] AHR is normally defined, as an increased sensitivity to airways to inhaled histamine or methacholine challenge test in the concert with a favourable response to a brief trial of conventional asthma therapy.[73,70] A positive methacholine test is defined as 20% reduction in forced expiratory volume in 1 second (FEV_1) with PC_{20} (Provocative concentration for a 20% fall in FEV_1) of methacholine less than 1.4 µmol/L. A methacholine challenge test is indicated when asthma is a possibility but when spirometry before and after bronchodilator use is not diagnostic. [71]

Absolute contraindications for methacholine testing include severe airflow limitation (FEV 50% perdicted), recent (within 3 months) myocardial infraction or stroke, uncontrolled hypertension (systolic blood pressure above 200 mm Hg) and aortic aneurysm.

Methacholine testing has a positive predictive value upto 88% and a negative predictive value of 100% for cough variant

asthma.[71] Thus negative results from a Methacholine test precludes a diagnosis of cough variant asthma. A small proportion of patients with positive result from a Methacholine test have false positive result (more likely among those with bronchitis, allergic rhinitis, COPD, congestive heart failure and cystic fibrosis). Cough variant asthma is more likely however, when results of chest X-ray examination are normal and response to a brief trial of asthma therapy is positive.

Diagnostic criteria proposed by Japanese cough society for CVA and atopic cough are as follows: [17]

For CVA

1. Isolated chronic non-productive cough lasting more than 8 weeks.
2. Absence of a history of wheeze or dyspnoea and no adventitious lung sounds on physical examination.
3. Absence of postnasal drip to account for cough.
4. Normal FEV_1 (≥80% of predicted value) FVC (≥80% of predicted value) and FEV_1/FVC ratio (≥ 70%).
5. Presence of bronchial hyperresponsiveness causing 20% fall in FEV_1 with provocation concentration of methacholine (PC_{20}<10mg/ml).
6. Relief of cough with bronchodilator therapy.
7. No abnormal finding indicative of cough etiology on chest radiograph.

For atopic cough

1. Non productive cough, lasting more than 8 weeks without wheezing or dyspnoea.
2. Presence of one or more finding indicative of atopy including past history and/ or complications of allergic diseases (excluding asthma) a peripheral blood eosinophilia (≥ 6% or =40 cells/μL) raised total IgE level in the serum (≥ 200 iu/ml) positive specific IgE antibody to aeroallergen and positive allergen skin test and /or induced sputum eosinophilia (≥ 2.5%).
3. Bronchial responsiveness within normal limits (provocation concentration of methacholine causing 20% fall in FEV_1, PC_{20} ≥ 10 mg/ml).
4. No bronchial reversibility defined as less than a 10% increase in forced expiratory volume in 1 sec (FEV_1) after inhalation of 300/ug sulbutamol sulphate following intravenous administration of 250 mg Aminophylline.
5. Increased cough receptor sensitivity [Capsaicin concentration eliciting 5 or more coughs (C_5) ≤ 3.9/uM].
6. Cough resistant to bronchodilator therapy (Oral clenbuterol 40/μg/day plus inhaled Salbutamol at bedtime and on demand) for ≥ 1 week.
7. No abnormal finding indicative of cough etiology, on chest radiograph.
8. Normal FEV_1(≥ 80% of predicted value) FVC (≥ 80% of predicted value) and FEV_1/FVC ratio (≥ 70%).

Differential diagnosis

In initial evaluation of the chronic non productive cough in children and adults with apparently normal chest X-ray the following diagnosis may be considered.[25]

In children

• Asthma	• Atopy/Allergic reaction
• Bronchiectasis	• Retained foreing body
• Infection	• Congenital malformation
• Irritant inhalation	• Postnasal drip
• Sinusitis	

In adult

• Infection	• Gastrooesophageal reflux
• Asthma	• left ventricular failure
• Postnasaldrip	• Carcinoma of lung (endobronchial)
• Sinusitis	• Tracheoesophageal fistula
• Chronic bronchitis	• Smoking
• Atopy/allergic reaction	• Eosinohilic bronchitis
• Irritant inhalation	• Idiopathic cough[72]
• Use of ACE inhibitor	• Interstitial lung disease

Treatment

The treatment of Cough Variant asthma is not different from that of typical asthma. Inhaled β-agonists have become the first line treatment modality in asthma therapy and are particularly convenient in the control of occasional exacerbations of cough, although in some patients they may stimulate coughing.[7] Most often, patients with CVA respond well to bronchodilators and corticosteroids drugs. Early introduction of inhaled corticosteroid (ICS) may lead to better prognosis in CVA by inhibiting airway responsiveness and airway inflammation as in case of classic asthma.[45,46]

Although, studies have indicated that cough variant asthma is generally mild and rarely needs intense therapy, oral steroid in short course is reasonable in refractory CVA.[12]

Patients with atopic cough responds poorly to inhale bronchodilator but they respond well to inhaled steroid and H_1 receptor antagonist eg. Azelastine.

The few patients who are refractory to inhaled steroid therapy do well with oral corticosteroid. Inhaled cromlyn sodium is useful as a prophylatic agent in CVA.[7] In addition to stabilising mast cell membrane, decreasing migration of eosinophil and inhibiting activation of neutrophils, cromolyn protects against sensitivity to changes in temperature and physical activity.[7]

The role of Montelukast, a cysteinyl-leukotriene receptor antagonist has been evaluated and have been shown that CVA symptoms can effectively improve if Montelukast is instituted early but late initiation of treatment with Montelukast treatment in the early phase after onset would have a greater long term clinical efficacy and might prevent the development of classic asthma.[73]

A recent report adds a possible new possible treatment option with Cilostazol, a Phosphodiesterase-3 inhibitor. The authors documented a significant increase in cough threshold after treatment suggesting that eilostazol might be an effective therapy for cough symptoms in CVA though it still requires further study.[74]

Furthermore, some investigators have claimed that avoidance of relevant allergen eg. dogdender, in addition to drug therapy may help to prevent progression to classic asthma symptoms.

Prognosis

Studies have indicated that substantial number of patients who initially present with CVA eventually develop mild to moderately severe manifestations of classic asthma with dyspnoea, prolonged expiration and wheezing during acute exacerbations.

In various studies, children with CVA wheezing developed with a prevalence of 9% to 75% during a follow-up period of 6-96 months.[75] In adult patients, Carrao[16] reported that wheezing developed in 33% of CVA patients within 18 months of diagnosis. Similarly, Braman et al[76] also found that wheezing developed in 38% patients within 3.0 to 5.5 years.

Regarding remission of CVA one study[75] showed that, 50% of patients with CVA had a resolution of cough within one month of bronchodilator therapy. They did not have recurrence of symptoms or need for further medication. Other report[22] revealed that, 20% patients achieved remission, defined as no recurrence of cough due to CVA for at least one year in absence of treatment. Patients of younger age group and lower airway reactivity showed higher rate of remission.

Nakajima et al[77] followed patients with CVA for 5 years and found that, 35% of them developed asthma with wheezing. There was no statistical difference in PC_{20} (Provocative dose of methacholine that cause 20% drop in FEV_1) between these two groups but rather it was the duration of cough that determined the outcome. The patients were treated with β-agonist/ Theophyline and not with inhaled steroid.

Use of inhaled Corticosteroid has been found significant effect on outcome of CVA patients. In a recent report by Fujimara et al has shown that among patients with CVA treated with ICS (Inhaled Corticosteroid) only 6% progressed to classic asthma compared to 30% patients without ICS treatment.[17]

Outcome of atopic cough, as defined earlier is much favourable and chance of developing classic asthma from atopic cough is significantly less compared to CVA.[17]

Conclusion

Cough variant asthma is a leading cause of chronic non-productive cough in both adults and children and is a precursor of asthma but remains a diagnostic challange because history, physical examination and simple spirometry results often fail to uncover abnormalities in lung mechanics.

Although the underlying pathophysiology of CVA is not clear but Airway Hyper-reactivity (AHR), that results from both airway constriction and inflammation, interact to stimulate the cough receptors to produce non productive cough without causing sufficient airway narrowing to produce wheezing which is characteristic of classic asthma.

Physicians should consider referring patients with undiagnosed chronic non-productive cough with unremarkable physical finding, normal chest x-ray and normal lung function for methacholine challenge test to diagnose CVA. 'Atopic Cough' similar to CVA shows normal bronchial responsiveness to methacholine challenge test but increased coughing with capsacin.

CVA responds to bronchodilator therapy with relief of cough but atopic cough is usually resistant to such therapy but both conditions respond to steroid treatment.

Recognition of CVA is important because without treatment a substantial number of patients develop classic asthma with wheeze in future although the patients with atopic cough only rarely do so.

Early introduction of anti-inflammatory therapy especially steroid inhalers and possibly oral leukotriene receptor antagonist have proved useful in alleviating cough and slowing the clinical progression of this condition.

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Launching of New Products

Arovent

Montelukast 10 mg Tablet

Once daily asthma medication

Orion Laboratories Ltd. has launched Arovent tablet containing film coated Motelukast Sodium INN equivalent to Montelukast 10 mg. Montelukast is indicated for prophylaxis and chronic treatment of asthma, prevention of exercise-induced bronchoconstriction and relief of symptoms of allergic rhinitis. Dosage and administration in case of Adults (15 years of age and older): 10 mg tablet daily to be taken in the evening. In case of Children (6-14 years age): 5 mg tablet daily to taken in the evening, Children (2-5 years of age): 4 mg tablet daily to be taken in the evening. Arovent 10 mg tablet, each box contains two alu-alu blister strips of 20 tablets. Each tablet's MRP is 10/- Tk.

Xzema Cream

Fusidic Acid BP 2.0% Betamethasone Valerate BP 0.1%

get xzema... forget eczema

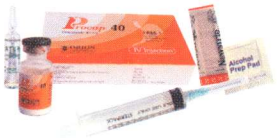
Orion Laboratories Ltd. has launched Xzema cream to cure Eczema. Each gram of Xzema cream contains Fusidic Acid BP 20 mg & Betamethasone as Valerate BP 1 mg. Xzema cream combines the potent topical antibacterial action of Fusidic Acid with the anti-inflammatory and antipruritic effects of Betamethasone. Betamethasone Valerate is a topical steroid with rapid effect in inflammatory dermatoses. Even refractory conditions can often be treated successfully. When applied topically, Fusidic Acid is effective against *Staphylococci, Corynebacteria, Neisseria* and certain *Clostridia* and Bacteroides. The antibacterial activity of Fusidic Acid is not diminished in the presence of Betamethasone. Xzema cream is indicated in inflammatory dermatoses where bacterial infection is present or likely to occur. Inflammatory dermatoses include atopic eczema, discoid eczema, stasis eczema, seborrhoeic dermatitis, contact dermatitis, psoriasis and discoid lupus erythematosus. In case of uncovered lesions 2-3 times daily applications and in covered lesions less frequent application may be adequate. Xzema cream is available as 10 gm tube at MRP Tk. 200/-.

Procap 40 IV Injection

Omeprazole 40 mg

The perfect solution to control severe acid secretion

Orion Laboratories Ltd. has introduced Procap 40 IV injection, each vial contains Omeprazole BP 40 mg (as Lyophilized Omeprazole Sodium BP). Procap inhibits secretion of gastric acid by blocking the hydrogen-potassium-adenosine, triphosphatase enzyme system, the so called 'proton pump' of the gastric parietal cell. It is an effective treatment for gastric and duodenal ulcers and particularly for erosive reflux oesophagitis. In patients with duodenal ulcer, gastric ulcer or reflux oesophagitis where oral medicationis inappropriate, Procap IV 40 mg once daily is recommended. In patients with Zollinger-Ellision syndrome the recommended initial dose of Procap 40 IV given intravenously is 60 mg daily. Higher daily doses may be required and the dose should be adjusted individually. When doses exceed 60 mg daily, the dose should be divided and given twice daily. Dose adjustment is not needed in patients with impaired renal function. As plasma half-life of Omeprazole is increased in patients with impaired hepatic function a daily dose of 10-20 mg may be sufficient. Dose adjustment is not needed in elderly patient. There is limited experience with Omeprazole 40 IV injection in children. Procap 40 IV injection should be given as slow intravenous injection. Solution for IV injection is obtained by adding to the 10 ml water for injection (WFI). Combi-pack containing 1 vial of 40 mg Omeprazole, 1 ampoule of 10 ml WFI and 1 disposable syringe (10 ml/cc) with an alcohol pad and first aid band. Procap 40 IV is available in attractive combi-pack in Tk. 70/- per pack as MRP.



Nosedex

Fexofenadine Hydrochloride USP

120 mg Tablet & 30 mg/ 5 ml Suspension

For rapid relief from allergic condition

Orion Laboratories Ltd. has launched, FDA approved treatment option for allergic rhinitis & urticaria, named Nosedex Tablet & Suspension. Each film coated tablet contains Fexofenadine HCl USP 120 mg and 5 ml Suspension contains Fexofenadine HCl USP 30 mg. Nosedex (Fexofenadine) is a long lasting H_1 receptor antagonist. Fexofenadine does not enter the brain from the blood and therefore does not cause drowsiness. Nosedex is indicated in Seasonal Allergic Rhinitis & Chronic Idiopathic Urticaria. Nosedex Tablet: In Seasonal Allergic Rhinitis & Chronic Idiopathic Urticaria, Adults and Children ≥12 years-60mg ($^1/_2$ tablet) twice daily or 120 mg (1 tablet) once daily or 180 mg once daily with water. Children 6 to 11 years-30 mg twice daily. Nosedex Suspension: Seasonal Allergic Rhinitis, Children 2 to 11 years-30 mg (5 ml or 1 tsf) twice daily. Chronic Idiopathic Urticaria-Children 6 to 11 years (5 ml or 1 tsf) twice daily. Children 6 months to less than 2 years of age-15 mg (2.5 ml or $^1/_2$ tsf) twice daily. Fexofenadine is generally well tolerated. Nosedex tablet: Each commercial box contains 3x10 tablets in blister pack,and MRP Tk. 6.50/- per tablet. Nosedex Suspension: Each bottle contains 40 ml suspension, and MRP Tk. 40/- per phial.

Ambronil 100 ml syrup

Ambroxol Hydrochloride BP

For easy expectoration

Orion Laboratories Ltd. has introduced Ambroxol Hydrochloride BP syrup under brand name 'Ambronil'. Each 5 ml of syrup contains Ambroxol hydrochloride BP 15 mg. Ambroxol is the active metabolite of Bromhexine and it has been proven that this metabolite possesses a greater bronchosecrotolytic effect than Bromhexine. Ambroxol is shown to exert 3 activities: 1. Secretolytic activity, 2. Anti-inflammatory and antioxidant activity, 3. Local anaesthetic effect. Indication: Productive cough, Acute and chronic inflammatory disorders of upper and lower respiratory tracts associated with viscid mucus including acute and chronic bronchitis, Inflammatory disease of rhinopharyngeal tract (laryngitis, pharyngitis, sinusitis and rhinitis) associated with viscid mucus, Asthmatic bronchitis, Bronchial asthma with thick expectoration, Bronchiectasis, Chronic pneumonia. Average daily dose (preferably after meal). Dosage and Administration: 2-5 years old - half teaspoonful (2.5 ml) 2-3 times a day, 5-10 years old: one teaspoonful (5 ml) 2-3 times a day and 10 years old & adults: two teaspoonfuls (10 ml) 3 times a day. Ambronil Syrup: Each PET bottle contains 100 ml syrup. MRP of each PET bottle Ambronil Syrup is 30/- Tk.

Dementia: Management update

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Introduction

Dementia is an acquired and persistent compromise in multiple cognitive domains that is severe enough to interfere with everyday functioning.[1] It is a syndrome consisting of a loss of several separable but overlapping intellectual abilities and present in a number of different combinations.[2] Dementia is a common, disabling and distressing neurological disorder and should not be considered a feature of normal aging. Many people reach old age without developing disabling cognitive impairment, although some aspects of cognition routinely change with age.[3]

Studies of aging, that address the epidemiology of dementia have revealed the presence of three groups of individuals: those who are cognitively normal, those who are demented and a third group that have cognitive impairment but do not meet criteria for dementia. These individuals may have impairment in a single domain, usually memory. This third group of patients cannot be classified as "normal" or as "demented", since the definition of dementia requires abnormalities in at least two cognitive domains and social or occupational disability. These individuals have been labeled as Mild Cognitive Impairment (MCI).[4] Patients with MCI are at increased risk for the development of AD. The annual incidence of AD in the general population ranges from 0.2% among those aged 65-69 years to 3.9% among those aged 85-89, but studies estimate the incidence rate among patients previously diagnosed with MCI to be between 6-25% per year. Early recognition of these patients will become increasingly important as treatments are developed that delay the transition from MCI to AD.[5]

A number of cognitive instruments have proven useful for screening of patients at risk for dementia. The Mini-Mental Status Exam (MMSE) is widely used. It is sensitive when scores are adjusted for age and education.[5, 6]

Stage of the disease by MMS

27-30	Normal
25-26	Possible
10-24	Mild-moderate
6-9	Moderate -severe
<6	Severe

There are four clinical dementia syndromes accounting for 90% of all cases after excluding other common reversible causes of cognitive impairment. These four major diseases are Alzheimer's disease (AD) and Vascular Dementia (VaD), which together account for approximately 80% of dementias, Dementia with Lewy body (DLB), and Frontotemporal Dementia (FTD). The clinician must rely on clinical criteria for making these diagnoses.

Alzheimer's disease

Alzheimer's disease is the most common cause of dementia among older adults. The natural course of AD averages 10 years. Memory decline is the hallmark of cognitive change in AD. The National Institute of Neurological and Communicative Disorders and Stroke-AD and Related Disorders Association (NINCDS-ADRDA) criteria for AD have been shown to have adequate sensitivity and specificity (see Table 1).

Table 1: NINCDS-ADRDA criteria for the diagnosis of alzheimer's disease [7]

I. Probable AD: core diagnostic features
- a. Dementia established by clinical examination (including MMSE, BRDRS, and neuropsychological testing).
- b. Deficit in at least two areas of cognition.
- c. Deficits characterized by gradual onset and progression, onset after age 40.
- d. Other systemic disorders or brain disease do not account for the progressive deficits in memory and cognition in and of themselves .

II. Possible AD: core diagnostic features
- a. Dementia syndrome in the absence of other neurologic, psychiatric, or systemic disorder, or
- b. Presence of a second systemic or brain disorder sufficient to produce dementia, which is not considered to be the primary cause of the dementia.

III. Features that make a diagnosis of probable or possible AD unlikely or uncertain
- a. Sudden apoplectic onset.
- b. Focal neurologic findings such as hemiparesis, sensory loss, visual field deficits, and incoordination early in the course of the illness.
- c. Seizures or gait disturbances at the onset or very early in the course of the illness.

IV. Criteria for diagnosis of definite Alzheimer's disease
- a. Clinical criteria for probable Alzheimer's disease.
- b. Histopathologic evidence obtained from a biopsy or autopsy.

Vascular dementia

Dementia due to cerebrovascular disease should be suspected when impairment in more than one cognitive domain accompanies clinical or neuroimaging evidence of stroke. Four sets of criteria exist for the diagnosis of VaD. None have been shown to have good specificity, but all are sensitive. Of these, the Hachinski Ischemic Score (Table 2) may identify the greatest number of patients with VaD in spite of not including neuroimaging criteria.[8, 9]

A score of = 4 is suggestive of AD or other non-vascular causes of dementia, while a score of = 7 is supportive of a diagnosis of VaD.

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Table 2 : Hachinski ischemic score [10]

Trait	Score
Abrupt onset	2
Stepwise deterioration	1
Fluctuating course	2
Nocturnal confusion	1
Preservation of personality	1
Depression	1
Somatic complaints	1
Emotional incontinence	1
Hypertension	1
History of stroke	2
Associated atherosclerosis	1
Focal neurologic symptoms	2
Focal neurologic signs	2

Dementia with lewy bodies

Dementia with Lewy bodies (DLB) has been defined clinically as a dementia syndrome with parkinsonism, delusions, hallucinations (especially visual), fluctuating alertness and sensitivity to neuroleptic medications (See Table 3).[11]

Table 3: Criteria for dementia with lewy bodies [9]

I. Progressive cognitive decline interfering with social and occupational functioning, usually including deficits of attention, frontal subcortical skills and visuospatial ability; memory impairment tends to be a later finding.

II. Two of the following core features are necessary for the diagnosis of probable DLB, one for the diagnosis of possible DLB.
- a. Fluctuating cognition with pronounced variations in attention and alertness.
- b. Recurrent visual hallucinations which are typically well-formed and detailed.
- c. Spontaneous motor features of Parkinsonism.

III. Supportive features
- a. Repeated falls
- b. Syncope
- c. Transient loss of consciousness
- d. Neuroleptic sensitivity
- e. Systematized delusions
- f. Hallucinations in other modalities

IV. A diagnosis of DLB is less likely in the presence of
- a. Clinical or neuroimaging evidence of stroke.
- b. Clinical, laboratory or neuroimaging evidence for other physical illness or brain disorder that accounts for the clinical picture.

Frontotemporal dementia

Frontotemporal dementia (FTD) features early behavioral changes preceding loss of memory, perception, spatial skills or praxis.[12] Onset of the disorder is typically between the ages of 45 and 65 years.

Table 4: Criteria for frontotemporal lobar degeneration[13]

I. Core diagnostic features
- a. Insidious onset and gradual progression
- b. Early decline in social interpersonal conduct
- c. Early impairment in regulation of personal conduct
- d. Early emotional blunting
- e. Early loss of insight

II. Supportive diagnostic features
- a. Decline in personal hygiene and grooming
  1. Mental rigidity and inflexibility
  2. Distractibility and impersistence
  3. Hyperorality and dietary changes
  4. Perseverative and stereotyped behavior
  5. Utilization behavior
- b. Speech and language
  1. Altered speech output
     - Aspontaneity and economy of speech
     - Press of speech
  2. Stereotypy of speech
  3. Echolalia
  4. Perseveration
  5. Mutism
- c. Physical signs
  1. Primitive reflexes
  2. Incontinence
  3. Akinesia, rigidity and tremor
  4. Low and labile blood pressure
- d. Investigations
  1. Neuropsychology: significant impairment of frontal lobe tests in the absence of severe amnesia, aphasia, or perceptuospatial disorder
  2. Electroencephalography: normal on conventional EEG despite clinically evident dementia
  3. Brain imaging (structural and/or functional): predominant frontal and/or anterior temporal abnormality.

Approach to dementia

Key points

- Determine presence of Dementia.
- Determine primary degenerative/other potential treatable causes of dementia.
- Co-morbid medical illness.
- Treatment of an intervening illness may reverse a worsening of dementia.

Diagnosis of dementia

- History
- Thorough clinical examinations

- Laboratory investigations

History of the patient in dementia [14]

a. Presenting illness

1. Onset
   - Early onset: e.g.
     CADASIL
     Deficiency states
     Postencephalitic
     SSPE
     Wilson's disease
     Leukodystrophy
   - Late onset: e.g. Alzheimer's disease (AD)
2. Duration
   - Long duration - AD
   - Short duration - Chronic subdural haematoma
     -Creutzfeldt-jakob disease (CJD)
3. Temporal progression
   - Slowly progressive - AD
   - Relentlessly progressive - CJD
     -Huntington's disease
     -Other infections

b. Past illness

- Gastric surgery - Vit. B_{12} deficiency
- Chancre - Neurosyphilis

c. Personal history

- Drugs - sedatives, tranquilizers
- Alcohol - thiamine deficiency
- I.V. drug users - HIV infection
- Working in chemical factory - lead, mercury

d. Family history

- HD
- AD
- Frontotemporal Dementia (FTD)
- Wilson's Disease
- CADASIL
- Some Hereditary Ataxias

Clinical examinations

a. Physical and Neurological examinations in dementia [14]

- AD: Does not affect motor system until late stage
- VaD: Hemiparesis, pseudobulbar palsy or other deficits.
- FTD: Axial rigidity, supranuclear gaze palsy
- Dementia with Lewy body (DLB): Parkinsonian features
- PSP: Unexplained falls, Axial rigidity
- CBD: Dystonia, asymmetric motor deficit, alien hand, Myoclonus.
- B_{12} deficiency: Myelopathy, Peripheral neuropathy
- Other Vit. deficiency and heavy metal poisoning: Peripheral Neuropathy
- Hypothyroidism: Dry cool skin, hair loss, Bradycardia
- HD: Chorea
- CRF: Anemia, HTN
- CLD: Features of portal hypertension, Palmar erythema, Gynaecomastia etc.
- Paraneoplastic e.g. Carcinoma bronchus - Clubbing
- Korsakoff's syndrome: Ophthalmoplegia, Confabulation,
- Neurosyphilis: Argyll Robertson pupil
- HIV infection: Opportunistic infections, Kaposis sarcoma
- Chronic lead poisoning: Blue lines in gums
- Arsenicosis: Mee's lines
- Wilson's disease: K. F. Ring

b. Cognitive and Neuropsychiatric examinations in dementia
Mini - Mental Status Examination (MMSE) is important for-

- Diagnosis
- Prognosis
- Treatment

Investigations in dementia [14]

a. Routine

1. Thyroid function test: e.g. Hypothyroidism
2. Serum Vit-B_{12} assay: Pernicious Anemia
3. Complete blood count (may give a clue)
   - Vitamin deficiency states.
   - Organ failure.
   - Endocrinopathies.
   - Neoplastic conditions.
   - Toxic causes. e.g., Basophilic Stippling of RBC in lead poisoning.
   - Vacuolated lymphocytes in Niemann: Pick disease.
4. Electrolyte: e.g. Increased K^+ in CRF, Addison's Disease
5. VDRL: Neurosyphilis, False positive in SLE.
6. CT/MRI of brain (MRI preferable in most cases)
   - Brain atrophy in different topography in different conditions.
   - Stroke, Binswanger's disease.
   - CNS infections.
   - ICSOL
   - Hydrocephalus
   - Leukodystrophies
   - Wilson's Disease
   - Hallervorden Spatz Disease

b. Optional focused tests

1. Chest skiagram
   - Cardiomegaly: Stroke, Hypothyroidism, Anemia,
   - Alcoholism
   - Ca. Bronchus
   - Pulmonary tuberculosis
   - Vasculitis: SLE, Wegener's Granulomatosis
   - Sarcoidosis
2. CSF study
   - CNS infections: e.g. HIV, Neurosyphilis
   - Decreased Aβ42: Amyloid & increased tau protein in AD- not diagnostic
3. Liver function tests
4. Renal function tests
5. Urine toxin screen: e.g. Lead, Arsenic, Mercury
6. Apolipoprotein: E genotyping in "AD"
7. DNA testing for ps-1-in "AD"

8. DNA repeats expansion (CAG) of Gene encoding Huntingtin on chromosome-4 diagnostic for HD.
9. Decreased Transkeltolase activity in Korsakoff's syndrome
10. Measurement of PrPsc in CJD: Diagnostic

c. Occasionally helpful
1. EEG
   - Repetitive bursts of diffuse high voltage sharp waves in CJD
   - Non convulsive seizure
   - Encephalopathies
2. Parathyroid function
3. Adrenocortical function
4. ESR: Vasculitis, CNS infections, Malignancy
5. Angiogram: Specially isolated CNS vasculitis
6. Brain & Meningeal biopsy
   - Not routine.
   - Isolated CNS vasculitis.
   - Potentially treatable neoplasm.
   - Young persons where diagnosis is uncertain.
7. SPECT
   - Not routine.
   - In atypical "AD": Hypometabolism & hypoperfusion in posterior temporo-parietal cortex.
8. PET: Almost exclusively a research tool.

Management of dementia[13, 15-21]

Supportive treatment

- ❑ Non-pharmacological
- ❑ Pharmacological

Treatment of complications & co-morbidities

Symptomatic treatment

General measures

Nutrition

- No special diet is required - unless they have Diabetes, Hypertension, Dyslipidaemia.
- A well balanced, nutritious diet is extremely beneficial
- Be sure to provide plenty of healthy fluids.

Creating a safer environment

- Because dementia can make daily activities more difficult, including eating, bathing, grooming, dressing, and using the toilet-it's important to modify the living environment to make it as easy as possible for the person with dementia to live and function.

Home safety

- Take a good look around your home, especially noting the physical layout and services that are available for support.
- Bathroom
  -The bathroom can be a dangerous place
  -Install grab bars in the shower or fold-down shower seats.
  -Use non-slip floor mats and slip-resistant tiles.
- Furniture
  -Move or remove objects, such as a loose throw rug, that could be a tripping hazard.
- Lighting
  -Be sure there is sufficient lighting.
  -Simplify furniture arrangements.

Driving

A person with Alzheimer's should not drive.

Tips for maintaining a normal life with dementia

- Keep a book to record important information, phone numbers, names, ideas, appointments, your address, and directions to your home.
- Label cupboards and drawers with words or pictures that describe their contents.
- Ask a family member to call and remind you of important things that you need to do in the day, like meal times, medication times, and appointments.
- Use a calendar to keep track of time and to remember important dates.
- Use photos of people you see often labelled with their names.

Exercise and dementia

- For people with Dementia, physical activity should be continued for as long as possible.
- Repetitive exercises - such as walking, indoor bicycling, and activities such as folding laundry - may decrease anxiety.
- The type of exercise that works best depends on symptoms, fitness level and overall health.
- Physical activity should be continued for as long as possible. This will help prevent muscle weakness and health complications associated with inactivity.
- Exercise also promotes a normal day and night routine, and may help to improve mood.
- Repetitive exercises-such as walking, indoor bicycling, and activities such as folding laundry.
- The type of exercise that works best depends on symptoms, fitness level, and overall health.

Caring for patient's personal needs

- People with dementia have special needs which can pose unique challenges for their caregivers.
- Depending on his or her level of independence the person with dementia may need help with personal care activities, including eating, bathing, shaving and using the toilet.
- To assist with these activities, caregivers need knowledge, skill and patience.
- Establish a routine. Schedule grooming activities for the same time and same place each day; for example, brush his or her teeth after meals or schedule baths for the mornings or evenings.
- Respect the person's privacy. Close doors and blinds. Cover the person with a towel or bathrobe.
- Keep in mind the person's abilities. Give him or her enough time to complete each task.
- Give the person encouragement and support as he or she completes tasks. Acknowledge his or her efforts when completed.
- Tell the person what you are doing. For example, "I'm going to wash your hair now".
- If the person can dress himself or herself, lay out the clothes in the order they are to be put on.
- Clothing that is easy to put on with few buttons, is the best.

Counselling and support

Crisis intervention counselling: In cases of emergency (such as initial despair over diagnosis), the counsellor will help get through the crisis.

Individual counselling: The person meets one-on-one with the counsellor. some problems are very personal and difficult to confront with others present.

Family therapy: A diagnosis of Alzheimer's disease or dementia can affect the entire family. Family therapy can help family members resolve issues among each other.

Group therapy: People join in a group and discuss their problems together. The session is guided by a counsellor. Members gain strength in knowing that they are not alone with their problems.

Long-term, residential treatment: The person receiving therapy lives at a treatment centre- hospitals, home-like structures, and clinics.

Self-help and support group: These include a network of people with similar problems. There are support groups for people with dementia and also for their families and caregivers.

Drug treatment of AD

The mainstay of treatment of AD, so far, is the cholinergic treatment strategies and most widely used, till now, are the CholinEsterase (Ch E) inhibitors.

Cholinesterase inhibitors (2 classes exist)

Class	Example		M/A
Class-I	Dual ChE inhibitors		Both AChE and BuChE
	Rivastigmine	Tacrine	
Class-II	Single ChE inhibitors		AChE
	Donepezil	Galantamine	

Medications used in the treatment of AD

Cognitive Agents	Starting Dose	Target Dose	Uses
Donepezil	5 mg daily	10 mg daily	Improve cognition may reduce apathy and hallucinations
Galantamine	4 mg BID	12 mg BID	
Rivastigmine	1.5 mg BID	6 mg BID	
Memantine	5 mg daily	10 mg BID	Slow functional decline, may improve agitation
Sertraline	25 mg daily	75-100 mg daily	Depression and agitation
Escitalopram	5 mg daily	10-20 mg daily	Depression
Trazodone	25 mg QHS	100-400 mg daily	Agitation, insomnia
Atypical Antipsychotics: Risperidone	0.25 mg daily	0.75-1.5 mg daily	Agitation, delusions, hallucinations
Olanzapine	5mg	10mg	Reduced psychosis and agitation
Quetiapine			Reduced psychosis and agitation
Vitamin E	1000 IU		delayed the onset of functional dependence and the need for institutionalization

Drugs to avoid in dementia

- Antipsychotics
  - Chlorpromazine
  - Clozapine
  - Promazine
  - Thioridazine
- Antidepressant
  - TCA
  - MAOIs
  - Paroxetine
- Anticholinergics
  - Benzhexol
  - Benztropine
  - Hyoscine
  - Orphenadrine
  - Procyclidine

Therapeutic target for the treatment of vascular dementia

- Improve cognitive impairments & hence general functioning.
- Improve behaviours, mood, psychosis or relational disturbances (Psychotropic).
- Arrest of slow worsening (secondary prevention).
- Control of risk factors in populations (primary prevention).

Cholinesterase inhibitors in vascular dementia

Treatment expectations from cholinesterase inhibitor therapy.

- Established
  - -Improve or slow decline in ADLs and cognition > 6 to 12 months.
  - -Stabilize cognition in moderate to severe dementia > 6 months.
  - -Efficacy in heterogeneous vascular dementia >6months.
- Not established or controversial
  - -Control most troublesome behavior.
  - -Delay the emergence of troublesome behavior.

Meantime in patients with VaD

- Meantime demonstrated beneficial effects in patients with VaD.

So, Meantime & AChEIs may play a role in the management of patients with VaD.

*Reversible causes require specific treatment accordingly.

Professional groups and some of their roles

Doctors: Evaluation of concurrent illness; prescription of medication; facilitating provision of hospital and community services.

Nurses: General care of in-patients and nursing home residents, carrying out behavior modification regimes, education and counseling of relatives, coordination of community services.

Clinical psychologists: Initiating behavior modification programmes, offering advice and support to staff in a caring role.

Social Workers: Facilitating provision of local authority services such as residential care, respite care, home care, counseling of cares.

Occupational therapists: Design of environment; education of carers, identification of strengths and abilities of patient.

Conclusion

The prevalence of dementia is rising as the aged segment of the population grows larger. Management of dementia should be

multidirectional, and is a complex and evolving task. A comprehensive approach is required that focuses on both the patient and his or her primary care giver. It is important to identify the type and stage of dementia. Supportive care and treatment of comorbidity are important, and common for all types. Treatable cause needs to be sought and sorted accordingly. Neurodegenerative dementias need symptomatic treatment with ChE inhivitors. Rivastigmine is possibly the best choice of ChE inhibitor so far and covers wider range for mild to moderate cases. Donepezile is a suitable and cheeper alternative. Memantine is being tried for moderate to severe cases. Current trials are focused on identifying reliable biological markers of dementia, preventing the advancement of MCI to AD and finding treatments to slow or halt the progression of AD and other dementing diseases.

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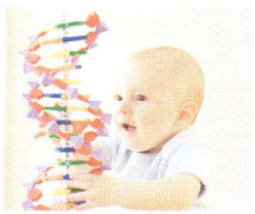
Medi News

Gene test more effective at detecting autism

Genetic factors increase the risk of developing autism spectrum disorder (ASD), but the specific genetic cause for an individual patient can be elusive. Genetic testing is crucial to identifying a cause for ASD in many children who do not have an easily recognizable genetic syndrome.

Current guidelines exist for two types of genetic testing - G-banded karyotype and fragile X DNA testing. In the study, "Clinical Genetic Testing for Patients with Autism Spectrum Disorders," published in the April issue of Pediatrics (released online March 15), researchers compared these two methods of genetic testing with a third method: chromosomal micr oarray (CMA). In a cohort of 933 patients with ASD, karyotype testing found 19 of 852 patients (2.2 percent) had abnormal genetic results, and fragile X testing was abnormal in 4 of 861 patients (0.4 percent). CMA identified abnormal results in 59 of 848 patients (7 percent), yielding the highest detection rate of the three tests.



Study authors conclude that CMA testing should be a first-tier test in patients with ASD. Establishing a clear genetic diagnosis may lead to earlier services for children with autism, and thus improved outcomes.

American Academy of Pediatrics

Resistant hypertension: An approach to its management

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Abstract

Resistant hypertension is defined as failure to achieve goal blood pressure (BP) when a patient adheres to the maximum tolerated doses of 3 antihypertensive drugs including a diuretic. Although the exact prevalence of resistant hypertension is currently unknown, indirect evidence from population studies and clinical trials suggests that it is a relatively common clinical problem and is projected to increase, owing to the aging population and increasing trends in obesity, sleep apnea, and chronic kidney disease. Analyzing available research on drug-resistant hypertension, the AHA's Professional Education Committee of the Council for High Blood Pressure Research found that 20 to 30 percent of patients with high blood pressure were unable to control their hypertension, despite treatment with three or more drugs. This clinical problem is faced by both primary care clinicians and specialists. Management of resistant hypertension must begin with a careful evaluation of the patient to confirm the diagnosis and exclude factors associated with "pseudo-resistance," such as improper BP measurement technique, the white-coat effect, poor patient adherence to life-style and/or antihypertensive medications. Education and reinforcement of life-style issues that affect BP such as sodium restriction, reduction of alcohol intake and weight loss if obese are critical in treating resistant hypertension. Exclusion of preparations that contribute to true BP treatment resistance, such as non-steroidal anti-inflammatory agents, cold preparations and certain herbs is also important. Lastly, BP control can only be achieved if an antihypertensive treatment regimen is used that focuses on the genesis of hypertension.

Definition and prevalence of resistant hypertension

Resistant hypertension is defined by a blood pressure of at least 140/90 mm of Hg or at least 130/80 mm of Hg in patients with diabetes or renal disease [(i.e., with a serum creatinine level of more than 1.5 mg per deciliter (133µmol per liter) or urinary protein excretion of more than 300 mg over a 24-hour period] despite adherence to treatment with full doses of at least three antihypertensive medications including a diuretic.[1] This definition does not apply to patients who have been recently diagnosed with hypertension. Moreover, resistant hypertension is not synonymous with uncontrolled hypertension which includes all hypertensive patients who lack BP control under treatment, namely, those receiving an inadequate treatment regimen, those with poor adherence as well as those with undetected secondary hypertension. High blood pressure that is under control, but requires four or more medications to treat it is also considered resistant to treatment. The prevalence of resistant hypertension in the general population is unknown. Studies, however, demonstrate a prevalence of resistant hypertension that ranges from 5% in general medical practice to > 40% in nephrology clinics.[2,3]

Prognosis of resistant hypertension

There are no sufficient studies addressed specifically to the prognosis of persons with resistant hypertension. However, evidences from studies on hypertension-related target-organ damage shows the risks of myocardial infarction, stroke, heart failure and renal failure directly in this group of patients with high level of BP.[1,4] Patients whose hypertension is uncontrolled are more likely to have target-organ damage and a higher long-term cardiovascular risk than are patients whose blood pressure is controlled.[5]

Factors contributing to resistant hypertension

There are many exogenous interfering factors that can contribute to the development of resistant hypertension. These include NSAIDs, anabolic steroids, sympathomimetic drugs (e.g., ephedra, phenylephrine, cocaine, and amphetamines), herbal supplements (e.g., ginseng and yohimbine appetite suppressants) etc.[6] Among these, NSAIDs and cyclo-oxygenase-2 inhibitors may raise both systolic and diastolic blood pressure by several mm Hg.[7] These agents impair the excretion of sodium, which causes volume retention; they also inhibit the production of local renal vasodilating prostaglandins; the therapeutic action of angiotensin-converting-enzyme (ACE) inhibitors and loop diuretics depends on the availability of these prostaglandins.[7,8] An assessment of dietary and lifestyle factors is also important. A high sodium intake (typically defined by a urinary sodium excretion of more than 150 mmol per day) and excessive alcohol use (more than three or four drinks per day) may contribute to resistant hypertension.[9,10] Studies show that more than 40 percent of patients with resistant hypertension are obese,[11,12] and obese patients may require higher doses of antihypertensive medications than do non-obese patients.

Pseudo-resistance

The term "Pseudo-resistance" refers to lack of BP control with appropriate treatment in a patient who does not have resistant hypertension. There are many causes of pseudo-resistant hypertension like improper blood pressure measurement, heavily calcified or arteriosclerotic arteries that are difficult to compress (in elderly persons), white-coat effect, poor patient adherence, complicated dosing schedules, inadequate patient education, memory or psychiatric problems, cost of medication, inadequate doses, inappropriate combinations, physicians inertia (failure to change or increase dose regimens when not at goal). Among these, suboptimal BP measurement technique, the white-coat effect and poor adherence to prescribed therapy are important. The possibility that an underlying condition is causing hypertension must also be considered because an evaluation study during an 18-year period at one tertiary center with 4000 patients showed 10% to 17% secondary causes.[13,14] The Identifiable secondary causes are- renal parenchymal diseases, renovascular diseases, primary Aldosteronism, pheochromocytoma, Cushing`s

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Syndrome, obstructive sleep apnoea, thyroid diseases, aortic coarctation, intra-cranial tumours etc.

Diagnosis and evaluations

Blood pressure should be measured after a patient has been seated quietly for five minutes with his or her arm supported at heart level and with the use of a properly calibrated and sized cuff. If the cuff is too narrow or too short, readings may be erroneously high (typically by 5 to 15 mm Hg in the case of systolic pressure). The patient should be asked whether he or she has smoked a cigarette within the previous 15 to 30 minutes, since smoking can cause an elevation in systolic blood pressure of 5 to 20 mm Hg.[15] Avoidance of coffee is also recommended, although the increase in systolic blood pressure after one cup of caffeinated coffee is usually only 1 to 2 mm of Hg.[16] The diagnosis is based on the findings of at least two or three elevated blood-pressure measurements (in the physician's office or at home), despite adherence to regimens containing three medications. However, if the blood pressure is above 160/100 mm of Hg, additional readings are not necessary for diagnosis.[1]

Evaluation (including physical examination and laboratory testing) is routinely warranted to look for evidence of end-organ damage related to hypertension and for other cardiovascular risk factors.[1] Volume overload and elevated sympathetic tone, which are common in patients with uncontrolled blood pressure, may occasionally be suggested by the presence of a rapid pulse rate.[17] The phenomenon of "white-coat," hypertension is very important here, because this is not benign and should not be ignored. Rarely, in older patients, inaccurate measurement of BP owing to severely sclerotic arteries appears to represent refractory hypertension. The presence of this condition can be confirmed by intra-arterial blood-pressure measurement.

Treatment of resistant hypertension

The rationale for intervention in resistant hypertension is to ensure that all possible mechanisms for BP elevation are blocked. So treatment of resistant hypertension focuses on several components. These include maximizing therapeutic lifestyle changes, withdrawing any medications or substances which may contribute to elevated blood pressure, treatment of secondary causes, maximizing medication adherence and focusing on pharmacologic modalities to achieve target blood pressure.

Non-pharmacologic treatment focuses on weight loss, dietary salt restriction (100mEq/24 hours), decreased alcohol ingestion, increased physical activity and ingestion of a high-fiber, low-fat diet rich in fruits and vegetables.

The timing of medication administration can affect blood pressure control. Switching one medication to bed-time than to taking all on awakening resulted in significantly reduced 24-hour systolic and diastolic blood pressures by 21.7% to 37%.[18]

As volume expansion seems the most frequent pathogenic finding in these patients,[19] an appropriate diuretic to decrease volume overload remains a cornerstone of therapy.[20] Studies suggest that changes in diuretic therapy (adding a diuretic, increasing the dose or changing the diuretic class based on kidney function) will help > 60% of these patients achieve BP goals.[19] Thiazide diuretics are effective from doses of 12.5 mg/day if kidney function is normal and an increase up to 50 mg may provide additional BP reduction in some patients.[21]

Of note, there are differences between thiazide and thiazide-type diuretics.[22] A recent trial comparing hydrochlorothiazide 50 mg and chlorthalidone 25 mg daily demonstrated that the latter provided greater ambulatory BP reduction, with the largest difference occurring overnight.[23] Additionally, a small study of patients with resistant hypertension demonstrated that switching from the same dose of hydrochlorothiazide to chlorthalidone resulted in an additional 8 mm Hg drop in systolic BP and increase in the number of subjects at goal.[24] Unfortunately, chlorthalidone is not commonly available in fixed-dose combinations; therefore, its use will require separate prescriptions.

The most crucial part of diuretic therapy is to know when kidney function has deteriorated, so that one may select the proper class of diuretic. For thiazides, this deterioration is generally thought to have occurred when the estimated glomerular filtration rate (eGFR) falls to < 50 ml/min/1.73 m^2, chlorthalidone can still be effective to an eGFR of 40 ml/min/1.73 m^2 if hypoalbuminemia or hyperkalemia is not present. For patients with eGFR < 40 ml/min/1.73 m^2, a loop diuretic should be used.[21] Frusemide or bumetanide must be given twice daily and possibly thrice daily in some cases, as they have short durations of action of 3-6 hrs. Thus once-daily use is associated with intermittent natriuresis and consequent reactive sodium retention mediated by increases in the RAS.[21] The loop diuretic torsemide has a longer duration of action and may be given once or twice daily.[21]

Use of the other drug classes in patients with resistant hypertension should be based on the general principles of combination therapy, namely inhibition of different pathogenic mechanisms, choice of drugs that will compensate for possible patho-physiological changes evoked by the first drug and consideration of compelling indications.[21] Moreover, the Food and Drug Administration has recently approved 3 fixed-dose combination antihypertensive agents for use as first-line therapy. These combinations all have an agent that blocks the RAS. Fixed-dose antihypertensive combinations are also very useful for patients with resistant hypertension, especially for those with adherence problems.[25,26]

The best combination of agents needed to achieve BP goal depends on patient characteristics (age, probable pathogenic mechanisms involved and concomitant diseases). In general, most patients should be on a blocker of the RAS along with a calcium antagonist and an appropriately dosed diuretic, especially for patients with increased weight and for appropriate time intervals.[27] If BP remains above goal, the next step is to add a fourth agent; a vasodilating beta-blocker is a good choice if pulse rate is not too low. Peripheral alpha-blockers are well tolerated and can be used. A combination of complementary calcium channel blocker (CCBs) also results in additive BP reduction.[28] Combining an angiotensin-converting enzyme (ACE) inhibitor with an angiotensin receptor blocker (ARB) shows to be less effective in terms of BP reduction than to adding a diuretic or a CCB to an ARB.[29]

Aldosterone is also part of the RAS and specific blockade of aldosterone should be considered in certain settings like obese or who have sleep apnea.[30] Amiloride is another potassium-sparing diuretic associated with BP reductions in patients with resistant hypertension.[31] Epleronone, a selective mineralocorticoid antagonist also has demonstrated BP-lowering efficacy as well as benefits on kidney disease progression. If BP control is still not achieved with full doses of a 4-drug combination, use of other agents such as centrally-

acting alpha-agonists (methyldopa and clonidine) or vasodilators (hydralazine or minoxidil) is needed. It must be noted, however, that if therapy has progressed to adding a fourth agent, referral to a clinical hypertension specialist is warranted.[32]

Endothelin-receptor antagonists (ERAs) also prove useful for resistant hypertension. Darusentan, a selective ERA recently tested in 115 patients with resistant hypertension, demonstrated a dose-dependent decrease in BP.[33]

So, pharmacologic treatment concentrate on use of an appropriate diuretic with a thiazide diuretic for most patients with preference to chlorthalidone and a loop diuretic for those with a decreased GFR. One recommended treatment option is a combination of a diuretic (thiazide) with an ACE inhibitor or ARB and a long-acting CCBs with or without a complimentary CCBs.

Additional fourth, fifth, and sixth line agents can be added based on individual patient characteristics with consideration given to treatment recommendations outlined by JNC VII. Other agents which should be considered include a mineralocorticoid antagonist, a combination alpha-beta blocker over a pure beta blocker or direct vasodilating agents (hydralazine or minoxidil).

Referral

Referral to a hypertension specialist should be considered in patients whose hypertension is difficult to control despite an assessment of adherence, dose, and other factors that may exacerbate the condition particularly if the use of the above mentioned combinations is not helpful.

Steps to tackling resistant hypertension

An expert panel at the American Heart Association has issued the following guidelines to help doctors diagnose and treat resistant hypertension.[34]

1. Confirm treatment resistance

- Patients with clinic blood pressure >140/90 (or >130/80 mm of Hg in patients with diabetes or chronic kidney disease), and prescribed three or more antihypertensive medications at optimal doses.
- Patients with clinic blood pressure at goal but requiring four or more antihypertensive medications.

2. Exclude pseudo-resistance

- Look into the patient's adherence to the prescribed regimen.
- Obtain home, work, or ambulatory blood pressure readings to exclude white-coat effect.

3. Identify and reverse contributing lifestyle factors

- Obesity
- Physical inactivity
- Excessive alcohol consumption
- High-salt, low-fiber diet

4. Discontinue or minimize interfering substances

- NSAIDs
- Sympathomimetics (diet pills, decongestants)
- Stimulants
- Oral contraceptives
- Licorice
- Ephedra

5. Screen for secondary causes of hypertension

- Obstructive sleep apnea (snoring, witnessed apnea, excessive daytime sleepiness).
- Primary aldosteronism (elevated aldosterone/renin ratio).
- Chronic kidney disease (creatinine clearance <30 ml/min).
- Renal artery stenosis (young female, known atherosclerotic disease, worsening renal function).
- Pheochromocytoma (episodic hypertension, palpitations, diaphoresis, headache).
- Cushing's syndrome (moon facies, central obesity, abdominal striae, inter-scapular fat deposition).
- Aortic coarctation (differential in brachial or femoral pulses, systolic bruit).

6. Pharmacologic treatment

- Maximize diuretic therapy, including possible addition of mineralocorticoid receptor antagonist.
- Combine agents with different mechanisms of action.
- Use of loop diuretics in patients with chronic kidney disease and/or patients receiving potent vasodilators (e.g. minoxidil).

7. Refer to specialist

- Refer to appropriate specialist for known or suspected secondary causes of hypertension.
- Refer to hypertension specialist if blood pressure remains uncontrolled after 6 months of treatment.

Conclusion

Although, the number of patients who cannot achieve BP goals on a regimen of multiple medications is growing, the phenomenon of resistant hypertension is widely under-studied. This requires treatment recommendations on the basis of pathophysiological principles and clinical experience. Effective management of resistant hypertension requires, first, a careful examination as well as exclusion of factors associated with pseudo-resistance, and second, identification and modification, if possible, of factors related to true BP elevations. Optimization of drug therapy designed to compensate for all mechanisms of BP elevation in a given patient and most importantly to control volume overload with proper use of diuretics, will help effective BP control for the majority of patients. To improve the long-term clinical management of this disorder expanded understanding of the causes of resistant hypertension and potentially more effective treatment is essential.

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A case report: Healthy pregnancy following removal of dermoid cyst

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Abstract

Dermoid cyst is the commonest Teratoma. It makes up to 10-15 percent of all Ovarian Tumour and tends to occur at a relatively early age. It is bilateral in 12 percent cases structures in a cystic Teratoma are predominantly ectodermal but there may be endodermal and mesodermal tissue as well.

Introduction

Ovarian tumours are quiet and rarely give rise to symptoms, excluding those which have an endocrine function. An abdominal swelling may be noticed by the patient or discovered during Routine Medical Examination. A Benign tumour is never painful unless complicated by torsion of the Pedicle.

Macroscopic feature, wall is mainly lined by stratified squqmous epithelium but there may be transitional and ever Columnar Epithelium. Structure in a Cystic Teretoma are predominantly ectodremal.

Case history

Mrs Shelly 20 years, para-0, house wife attended to me with the history of lump in lower abdomen for 1 year with primary sub fertility. There was no abnormality in menstrual cycle. She had no family history of Breast, Ovarian or Colonic cancer. On general examination no abnormality was detected. Abdominal examination revealed Foctal head size lump in the supra pubic region, 10 cm in diameter having smooth surface and no Foctal tenderness. There was no Ascites and no enlarged Lymph Nodes. On Bimanual examination tumour felt through anterior fornix, separated from the Uterus and the Uterus was of normal size. Diagnosis was confirmed by:

1. USG which showed loculated 12x12 cm hypoechoice solid mass with thin septum in the left adnexae.

2. Straight x-ray of the abdomen showed teeth within the cyst.

After doing all routine investigation and proper counseling with the patient and her relative laparotmy was done in Saturia Nursing Home, in the district of Manikganj in 2004. Laparotomy was done by midline incision and a Foctal head size ovarian tumour was found, pedicle of which was twisted, but the pedicle was healthy and right sided ovary and tube was healthy. Accordingly left sided Salopingo-oophorectomy was done, preservation of right ovary and Fallopian tube. Histopathology revealed mature cystic teratoma. Post operative period was uneventful and patient was discharged from the clinic at 7th Post Operative day with the advice not to conceive within at least 6 months.

Patient conceives after 1 year, and again came to me. Regular Antenatal Check Up was done. Anomaly scan was done at 18-20 weeks and was found everything normal. Seven days before E.D.D patient was admitted in Saturia Nursing Home and as the patient was short statured and due to Cephalo-Pelvic disproportion elective Caesarian Section was done and a healthy Male baby was extracted weight 3.5 kgs, Apgar score and other reflexes of the baby were normal. She was discharged from Nursing Home on 5th P.O.D and was adviced to come after one and half month later.

She was then clinically evaluated and found completely ok.

Conclusion

Dermoid cyst is a Benign Cystic Teretoma, but it may become malignant in 1 to 2 cases. Early diagnosis, early laparotomy and histopathology makes the patient almost cure.

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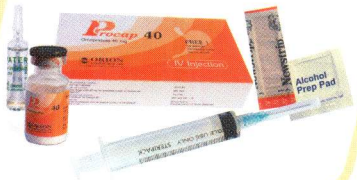
Omeprazole

Procap

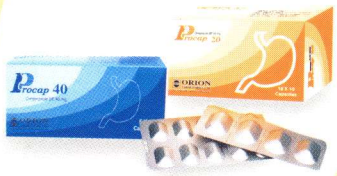
20 mg / 40 mg Capsule &
40 mg IV Injection

Protection from hyperacidity

Emergency therapy



Sequential therapy



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